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BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

Vol. 39.] 1942. [No. 4.

SUMMARY OF RECENT ABSTRACTS.*

III. MALARIA.

[*Continued from* p. 137.]

Treatment.

REED (p. 291) has written a paper on the treatment of malaria which, being too comprehensive for abstract, should be consulted in the original. In comment, WHITE draws attention to a misstatement of the dosage of plasmoquine.

FORBES (p. 177) points out that quinine has a predilection for the auditory nerve, and states that there is clinical and experimental evidence that quinine administered to the mother during pregnancy may cause deafness or amblyopia in the child. He gives figures which indicate that the taking of quinine over long periods of time may cause nerve deafness but not other forms. LYNCH and BRANDT (p. 291) describe a case of accidental quinine poisoning in a child.

WILKINSON (p. 337) reports three cases in which mental disturbance followed the taking of atebrin; all the patients recovered rapidly. BALLERO (p. 34) reports favourably on Italchina, a new acridine derivative stated to be effective against all forms of malaria.

CANNISTRACI (p. 33) states that in Messina no relapses occurred in 192 cases of malaria after two courses of atebrin and plasmoquine.

In the *Annals of Tropical Medicine and Parasitology* (p. 508) are recorded tests which indicate that pamaquin (I.C.I.) is identical with plasmoquine. NANDI (p. 645) discusses the respiratory metabolism of certain tissues in the presence of plasmoquine.

The intravenous administration of reconstituted serum produced striking improvement in a patient suffering from severe subtertian malaria, which did not respond to atebrin and quinine. FAWCITT and WALTERS (p. 508), in reporting the case, discuss the possible mode of action of the serum.

FIELD (p. 35) states that Certuna has an effect on gametocytes of *P. falciparum* similar to that of plasmoquine, but has no effective action on asexual forms of that parasite, or on any form of *P. vivax*. He reports unfavourably on certain other new drugs.

* The information from which this series of summaries has been compiled is given in the abstracts made by the Sectional Editors in the *Tropical Diseases Bulletin*, 1941, Vol. 38. References to the abstracts are given under the names of the authors quoted, and the pages on which the abstracts are printed.

COLE *et al.* (p. 178) describe the action of sodium bismuth thioglycollate in therapeutic benign tertian malaria induced by blood inoculation. This drug contains 38 per cent. of bismuth and is given intramuscularly in doses of 0·2 gm. In therapeutic malaria, when the fever is prolonged and remittent, a single dose usually procures a 48-hour respite from fever, after which paroxysms return on alternate days, or the drug may transform a quotidian to a tertian fever. Repeated injections can arrest malaria for long periods, and the drug is useful in thus interrupting the fever in those in whom it is desirable that recovery from the more alarming symptoms should take place without abolition of the infection ; it is not a substitute for quinine.

DE LEON (p. 712) states that sulphanilamide may be useful in acute attacks of subtertian malaria in which intravenous medication is indicated ; it is exclusively schizonticidal. PAKENHAM-WALSH and RENNIE (p. 231) report that sulphathiazole produced a great reduction in blood parasites in a patient who had been inoculated with *P. vivax*.

STEPHENSON (p. 292) records great improvement in 11 cases of malarial splenomegaly treated by the Ascoli method, but little improvement in 7 others with splenomegaly due to other causes. NUCCIOTTI (p. 107) has devised a new method of administering adrenalin for the treatment of malaria, and uses Surrenasi, an extract of whole adrenal gland containing adrenalin, cortical hormone and vitamin C, for this purpose. The dose is 0·01 mgm. intravenously daily for 6 days, followed by 0·02 mgm. daily for 6 days, and the drug is given in association with quinine treatment. This is claimed to be more effective than the Ascoli method and the total adrenalin is only 0·18 mgm., little more than one-tenth of the amount given in the Ascoli course.

Drug prophylaxis.

[Most of the work reported below was done on estates in the Far East. It is not unlikely that a proportion of the labourers concerned possessed some immunity against the strains of malaria commonly found there ; whether similar results could be achieved in Europeans and other non-immune persons, under the conditions of modern war, cannot be deduced from these results, but it seems probable that drug prophylaxis may be of such value that it cannot safely be neglected. Of the drugs used, atebrin appears to be the most satisfactory.]

FARINAUD (p. 108), in a consideration of the results of drug prophylaxis in Indo-China, comes to the following conclusions :— If the breeding of the principal vectors is not controlled in hyperendemic areas, drug prophylaxis cannot confer complete or lasting benefit. If the population concerned possesses some immunity, or if the density of the vectors is reduced, drug prophylaxis may be of great value. It is the best method of dealing with sudden increases in malaria in areas of sporadic or epidemic malaria. The basis of drug prophylaxis is quinacrine [atebrin], and the addition of gametocides does not add appreciably to its efficacy. BARROWMAN (p. 231) makes the point that for drug prophylaxis to be effective the population under treatment should not exceed 100. In his opinion the case rate and death rate may be reduced, but such reduction, in estate communities, cannot compare with that achieved by anti-mosquito measures. Certain strains of malaria parasite do not respond to

atebrin. STRAHAN (p. 231) considers that on estates where anti-mosquito measures fail to protect the labour lines, drug prophylaxis should be given a trial.

MOOIJ (p. 512) advises the use of prophylactic quinine in the army in the Netherlands East Indies; the dose of 6 grains daily, though it will not prevent infection, will modify the severity of the attacks. LAMPRELL (p. 179) writes favourably of the results obtained by drug prophylaxis with atebrin and with quinine in an estate in Assam where mosquito control was not practised at the time. He stresses the finding discussed below by FIELD and NIVEN, that after cessation of the drug administration there is a higher incidence in treated than in control groups, and that this is especially marked when atebrin is the drug employed.

FIELD (p. 35) states that atebrin given to estate labourers in Malaya in doses of 0·3 gm. once each week was more effective in reducing the incidence of clinical malaria than the same drug given in doses of 0·3 gm. for 5 successive days every 5 weeks. In a severe epidemic of tertian malaria in Alabama, TATE (p. 105) notes that the issue of atebrin as a prophylactic, 0·2 gm. twice each week, afforded relief, and that during the period of this administration clinical cases were few. CANNISTRACI (p. 33) recommends atebrin, in doses of 0·3 gm. once or twice each week, as a prophylactic for the people of Messina. Children support this dose.

CLARK *et al.* (p. 511) set out the conclusions they have reached as a result of their observations in the very complete 10-year experiment in drug prophylaxis conducted in Panama. Atebrin, or quinine, and plasmoquine have been given to all persons found infected at monthly surveys. They consider that by such means it is quite impossible to eradicate malaria parasites or to reduce them to the point at which transmission is greatly lessened. Drug prophylaxis cannot prevent an epidemic if unusually great numbers of Anopheles are present, but severe clinical malaria can be almost eliminated. Atebrin and quinine are equally effective, but atebrin is the easier to give; plasmoquine is probably of little assistance. A drug-control programme is economically justifiable in view of the increased labour efficiency which results. Figures of recent findings are given. [It would seem to be important to differentiate these results from others obtained by the continuous, regular, administration of drugs to whole populations, regardless of the presence or absence of parasites.]

FIELD and NIVEN (p. 107) have investigated the phenomenon, constantly observed in Malaya, of the rapid reappearance of clinical malaria which follows the suspension of the administration of prophylactic drugs to Indian labourers, whatever the time of year. The attacks, which often occur within a month of cessation of the drugs, are almost limited to non-immune immigrants, and are regarded as either delayed primary attacks contracted during the period of drug taking, or infections acquired a year or more before, and kept latent by the drug. Their severity is no greater than that of other attacks. It is concluded that effective drug prophylaxis is not consistent with the acquisition of effective immunity. The drugs employed are quinine and atebrin [the dose of the latter being 0·2 gm. on two successive days of each week. This is evidently of great value in suppressing clinical malaria in the population concerned.]

On an estate in the F.M.S., where the breeding of vectors is uncontrolled, the administration of plasmoquine in doses of 0·02 gm.

twice each week failed to bring about a reduction in the amount of malaria. FIELD (p. 35) reports that large numbers of carriers of gametocytes of *P. vivax* persisted, and that the incidence of infected mosquitoes remained approximately the same as during the previous year when schizonticidal drugs only were employed. KINGSBURY (p. 102) also reports unfavourably on attempts at drug prophylaxis, in which plasmoquine in doses of 0·02 gm., twice each week, were given on an estate in Malaya. The Italian drug M.3 was similarly unsuccessful.

Control.

General.—KEKHCHER (503) reports that in the peat bogs of the Province of Moscow, where *A. maculipennis* is the vector, control by systematic catching of adults in houses, and by the use of oil and Paris green, is insufficient and that medical treatment of the entire population is necessary in the spring.

In the Philippine island of Luzon, where *A. minimus* is the principal vector, MCMURDO (p. 333) records the protective measures used by troops on manoeuvres during 1940. Camp siting was realized to be important, mosquito nets were systematically employed, quinine was given in daily doses of 5 grains, and Bamber oil was used as a repellent. With these precautions it was found that the malaria records for 1940 were very low in comparison with those of 1938 and 1939. In the Netherlands Indies MOOIJ (p. 512) reports that, for the protection of troops, a recommendation has been made that mosquito screens should be made of wire with a mesh of 1·25 mm. and that mosquito nets should have at least 26 meshes to the inch.

For the labour camps and headquarter towns along the China-Burma road, WILLIAMS (p. 502) reports that control measures, consisting of subsoil drainage, the use of larvicides (oil, pyrethrum and Paris green), the shading of streams by means of bushes, and the use of Gambusia, should secure adequate protection, and thus remove the main dangers to health which have hindered road construction and the delivery of supplies.

GRANETT (p. 713) has carried out tests on a large number of mosquito repellents and gives information about those found to be useful, the best of which, a proprietary product known as Sta-Way Insect Lotion, contains diethylene glycol monobutyl ether acetate and diethylene glycol monoethyl ether, with ethyl alcohol, maize oil and perfume. Citronella oil and other preparations are ranked next in efficiency to this product.

STRAHAN (p. 231) points out that in Malaya, where oiling has been carried out conscientiously on estates, reasonable control of *A. maculatus* has not been achieved, and indicates that this is probably the result of a too rigid observance of the half-mile rule. The mosquitoes reach the labour lines from outside the protected zone in numbers sufficient to be dangerous. BARROWMAN (p. 231), however, insists that, in spite of criticism as to its adequacy, the half-mile rule remains the most important starting point in malaria control, but that it must be applied intelligently. He discusses fascine and pipe drainage.

Insecticidal sprays.—[Work on insecticidal sprays continues to show most encouraging results. It is a method of prevention which may have great value in military communities in many parts of the world.]

COVELL (p. 228) reports good results from the spraying of dwellings in India with pyrethrum insecticides. WATS and BHARUCHA (p. 234) note that for insecticidal spraying to be effective in dwellings which cannot be rendered relatively air-tight, the maximum concentration of insecticide must be secured in the minimum of time. They give details of an apparatus efficient in this matter. RUSSELL and KNIPE (p. 645) have continued their work on the spraying of dwellings in India with an insecticide of Pyrocide 20, one part, in nineteen parts of kerosene. The spraying is carried out once or twice each week, but a recent modification has been the spraying of the outside of the house, under the eaves, before entering to spray the interior. This is effective, and the authors give figures of spleen and parasite rates which show how valuable the whole procedure is. The cost is less than that of anti-larval work, but is high in relation to the economic level of the community.

DZHANGIROV (p. 179) has used a cold water infusion of tobacco dust, which contains 0·1 per cent. nicotine, as a spray for killing mosquitoes in cellars in the Caucasus region. He claims that 100 per cent. of the mosquitoes can be killed if soft soap is added to the strained infusion immediately before use. POGODINA and SOKOLOV (p. 510) write of the use of anabasine [an isomer of nicotine] as an aerosol for the destruction of anophelines. The minimum concentration which killed all the mosquitoes in a room in 8 minutes was 0·2 oz. per 1,000 cu. ft., a rate considerably smaller than that required for HCN. The aerosol has an unpleasant smell and causes coughing, so that the operator must be protected. Details of use must be sought in the original abstract.

CHOPRA *et al.* (p. 234) found that powdered leaves of *Tephrosia vogelii* from Assam have no larvicidal or insecticidal action, and that the action of a kerosene extract is due to the vehicle only. It had previously been reported that in Rhodesia the leaves had been found useful in these respects.

CHOPRA *et al.* (p. 645) state that the essential oil of *Artemisia vulgaris*, which grows abundantly in hilly districts of India, has insecticidal and larvicidal properties comparable with those of kerosene.

Water control.—RAMSAY and ANDERSON (p. 232) record their experiences with siphons in N. Bengal, for the control of *A. minimus*. Since a prolonged flush controls a greater length of channel than more frequent shorter flushes, large reservoirs are required; a total discharge of 50,000 gallons is the minimum amount necessary to control a mile of a channel 6 to 8 feet wide. The "Dooars" siphon was satisfactory, and its construction is not difficult. WORTH and SUBRAHMANYAM (p. 232) discuss the siphons used in Ceylon. With a head of 25 to 40 inches of water it should be possible to control a distance of 5,000 feet below the dam. Hand-operated gates may be preferable to automatic siphons where dry-weather flow is low.

Intermittent irrigation of rice fields in Portugal is carried out according to the cycle 10 days wet, 7 days dry. HILL and CAMBOURNAC (p. 564) state that in this way the number of mosquito larvae has been reduced by over 80 per cent., the amount of water needed for irrigation decreased, and usually the yield of rice increased without detriment to the quality of the grain. Special preparation of the fields is needed, but this is the only feasible measure of control so far evolved. RUSSELL and RAO (p. 559) state that intermittent irrigation of rice fields in S.E. Madras, 2 dry days and 5 wet, will prevent the breeding

of mosquitoes except during periods of daily rain. The planting of rice in irrigation channels themselves might control the breeding of *A. culicifacies* after the rice has attained a height of 12 inches above the water surface, and may do this without serious obstruction to the flow of water.

MONDAL (p. 564) gives an example of stream training for the control of *A. fluviatilis* and *A. varuna* in the Jeypore hills.

HOPKINS (p. 233) writes of afforestation as a useful procedure in the drying-up of swamps in Uganda, in which *A. gambiae* and *A. funestus* breed diffusely though not with great intensity. Swamps should first be drained and then afforestation with species of Eucalyptus may be carried out, with care that the spacing of the trees should be such as to produce the maximum leaf area. Ditches should be heavily shaded, and indigenous species of Ficus are useful for this. Residual pools should be filled in.

Oiling.—WATSON (p. 509) states that all the toxic substances in anti-larval oils are soluble in water and are capable of penetrating larval cuticle; the larval heart is very susceptible to these water-soluble toxins. He discusses the mechanism of the entry of oil into the spiracles.

CHOPRA *et al.* (p. 565) show that although the larvicidal action of pyrethrum powder in the field is slight, the action of kerosene is enhanced, and its spreading power increased, by the addition of pyrethrum. Aqueous extract of pyrethrum has insecticidal properties although the active pyrethrins are insoluble in water, and the insecticidal action cannot always be correlated with the pyrethrin content.

Paris green.—STAROSTIN (p. 509) in Russia has found that to be effective as a vehicle for the dilution of Paris green, road dust should flow easily. This capacity is found in those dusts which do not form lumps, are not easily reduced in volume when submitted to pressure, and are not hygroscopic. Sandy dusts, with little clay, are good, but much depends on the size of the sand particles. Sand from rivers or deserts is suitable, since the particles are polished and oval, whereas the grains from foothills or mountains are angular and more apt to form a compact mass.

Although aeroplane dusting of Paris green is impracticable in low-lying, densely populated areas near large rivers of the Smolensk region, where breeding places are small and scattered, LAZUK (p. 510) states that it is the most effective method of treating large turf pits in peat bogs, which are usually inaccessible for hand dusting. An additional measure of control consists of the spraying of dwellings with an emulsion of kerosene, soft soap and water. In the Tennessee valley, where the river has been impounded and transformed into a series of large reservoirs, BISHOP (p. 292) reports that Paris green applied by aeroplane at the rate of about one pound per acre has produced no catastrophic destruction of aquatic organisms important as fish food. Arsenic accumulates in the fish but not to an extent which renders them unfit for human consumption. Larvicidal oil and pyrethrum larvicide destroy a large proportion of amphipods.

RUSSELL *et al.* (p. 564) describe the procedure for the use of Paris green in suspension, with kerosene, egg albumin and water, which is sprayed on to the surface of water. By this means mosquito breeding may be effectively controlled even in the presence of considerable vegetation.

In a comparison of the larvicidal actions of a pyrethrum emulsion and a Paris green mixture, HENDERSON and HOWARD (p. 292) show that the former is much more expensive than the latter, to produce the same effect, and that it kills many invertebrate mosquito predators.

Fish.—VANDERPLANK (p. 565) describes certain small fish, closely allied to Gambusia, which are indigenous to East Africa and which should be of greater local value than Gambusia in malaria control. JOHN (p. 233) notes that the Indian top minnow *Aplocheilus lineatus*, common in Travancore, is a very useful larvivorous fish.

Malaria of Monkeys and Birds.

Monkeys.—It has often been stated that malaria runs a more severe course in people who are ill-nourished and in poor health than in those who are well fed and healthy. To test this view PASSMORE and SOMMERVILLE (p. 646) fed two groups of monkeys (*Macacus radiatus*), one group on a poor diet resembling that of poor human rice eaters, and the other on a generous and healthy diet. Great differences in general health were noticed, but it was found that injection of equal doses of *P. knowlesi* or *P. cynomolgi* into the members of the two groups produced little, if any, difference in reaction between the groups. The course and severity of the primary attacks were not affected by the state of nutrition.

MULLIGAN *et al.* (p. 648) have carried out experiments on monkeys which lead them to conclude that there are three agencies at work in the defence of the organism against malaria: first, an inherent quality of the host which is inimical to the development of the parasite; second, a cellular mechanism in the lymphoid-macrophage system, centred chiefly in the spleen; third, a specific humoral factor acquired as the result of infection. High natural immunity is not greatly affected by removal of the spleen, and depends, therefore, on inherent unsuitability of the body tissue. Poor natural immunity is almost abolished by splenectomy, and therefore depends upon the lymphoid-macrophage system. Details of the experiments with different species of monkeys and parasites are given. The same authors (p. 647) show that injection of homologous immune serum will slightly modify *P. knowlesi* infection in monkeys (except those from which the spleen has been removed), but not infection with *P. cynomolgi*. In monkeys previously infected with *P. cynomolgi*, and in which, therefore, the lymphoid-macrophage system has been stimulated, anti-*knowlesi* serum will definitely control *P. knowlesi* infection. Yet monkeys recovered from *P. cynomolgi* infection are as susceptible as normal controls to *P. knowlesi*. The conclusion is that defence mechanism involves the interaction of both cellular and humoral agencies. The same authors (p. 648) have obtained similar results by using saline extracts of malarial spleens in place of immune serum; this indicates that the immune substances are present in the spleen though not, apparently, in greater concentration than in the blood.

TALIAFERRO and KLÜVER (p. 412) have studied *P. brasilianum* infections of monkeys; they consider that the lymphoid hyperplasia in malaria augments the mesenchymal reserve from which monocytes and newly formed macrophages arise.

COGGESHALL (p. 293) has shown experimentally that definite immune bodies, capable of preventing infection when incubated with parasites

before injection into monkeys, occur in the serum of human beings who have recovered spontaneously from infections with *P. knowlesi*. Complement fixing bodies are also present, but there is no uniform correlation between their titre and the protective action of the sera.

SHORTT and MENON (p. 338) failed to produce any active immunity by the injection into monkeys of killed *P. knowlesi* freed from their host red cells.

SINGH and SINGH (p. 294) observed that when a suspension of washed red cells from *M. rhesus* infected with *P. knowlesi* was used, the serum from monkeys infected with the same parasite produced agglutination of the cells. Sera from animals infected with *P. cynomolgi* or *P. inui* would not agglutinate cells from animals infected with *P. knowlesi*. They (p. 294) have found that infection of *Macacus rhesus* with *P. knowlesi*, *P. cynomolgi* or *P. inui*, and recovery, protects against reinfection with the same parasite, but that cross immunity is not produced. The same authors (p. 294) have obtained some success in the treatment of *Macacus rhesus*, infected with *P. knowlesi*, by the injection of large quantities of serum from chronically infected animals.

SHORTT and MENON (p. 338) have succeeded in infecting monkeys with *P. knowlesi* and fowls with *P. gallinaceum* by the oral route, care having been taken not to injure the mouth during the administration.

DIKSHIT and GANAPATHI (p. 647) have used sulphathiazole successfully in *P. knowlesi* infection of monkeys.

Birds.—MULLIGAN and RUSSELL (p. 338) report that sporozoites of *P. gallinaceum* are agglutinated by normal sera of animals and man, more readily by sera of animals which have suffered from malaria, and most readily by sera of fowls chronically infected with the homologous parasite. These results are amplified in a later paper by MULLIGAN *et al.* (p. 646), who reach the conclusion that sporozoite agglutination in high dilutions (1/64 or more) of malarial serum is a specific reaction. Human malaria serum agglutinates sporozoites of *P. gallinaceum*. Details of technique are given.

SCHULEMANN (p. 35) has given a résumé of modern views on the development of exoerythrocytic schizonts in the malaria of birds.

PORTER and HUFF (p. 513) state that erythrocytic schizogony has been observed in strains of *P. relictum*, *P. gallinaceum*, *P. cathemerium*, *P. circumflexum* and *P. nucleophilum*, but not in other species of bird malaria parasite. Bodies resembling these schizonts have been seen in monkey and human malaria (*P. vivax* and *P. falciparum*). The authors, from a review of the literature, conclude that although direct development from sporozoites occurs, the schizonts may arise from erythrocytic forms. MANWELL (p. 513) notes that exoerythrocytic schizogony is found in infections with *P. relictum* var. *matutinum*, and that this form of parasite has been found in a canary infected by means of a single erythrocytic parasite, a conclusive proof that the exoerythrocytic form may arise from the usual blood form.

SHORTT *et al.* (p. 413) have inoculated very young chicks, or chicks still within the egg, with sporozoites of *P. gallinaceum*. Their observations lead them to think that sporozoites enter the blood and are taken up by, or actively enter, the endothelial cells. They multiply by schizogony and increase in numbers until merozoites enter red cells to become pigmented forms. Exoerythrocytic schizogony continues as a low grade infection not visually detectable until it is stimulated to further development and causes a relapse of the pigmented forms.

It is usually assumed that malaria persists as a low grade infection with pigmented forms, but the authors put forward the view that it may be merozoites from exoerythrocytic schizonts which are responsible for cases of malaria infection in which gametocytes are the only blood forms present.

SCHULEMANN and SPIES (p. 294) quote evidence, from experimental work, which proves that pigment-free exoerythrocytic schizonts which arise directly from sporozoites, in birds, are contained in histiocytes. Further development takes place either intra- or extra-cellularly; intra-cellular development may be within the histiocytes, when pigment-free forms are found, or in the red cells, when pigmented forms are produced.

COULSTON and MANWELL (p. 512) have produced infection with *R. circumflexum* in a single red cell isolated by micro-manipulation or dilution methods. From such infections, exoerythrocytic schizonts have developed, though not in the first birds infected, and it is therefore evident that pigmented forms existing in red cells can give rise to non-pigmented forms, but these are probably only found when the defensive mechanism of the host is severely taxed, as it is by a massive dose of parasites.

HEWITT (p. 295) remarks that if exoerythrocytic schizogony is part of the life-cycle of some avian malarial parasites the factors which govern its appearance are unstable; such schizonts have never been found in one strain of *P. cathemerium*, even after exhaustive search, though they occur readily enough with other strains of the same parasite.

In canaries infected with *P. cathemerium*, HEGNER (p. 296) shows that the observed daily increase in the number of parasites is well below that which would be expected on the basis of the average number of merozoites produced at schizogony. An increasing percentage of parasites is destroyed each day, which indicates that immunity is acquired gradually, and does not appear suddenly at the crisis. Human and monkey malaria appears to be similar to that of birds in this respect. GINGRICH (p. 650) points out that in *P. cathemerium* infection, two-thirds of the merozoites fail to survive. From experiments on the blocking of the reticulo-endothelial system in this infection he reaches the conclusion that natural immunity, as evidenced by the failure of numbers of parasites to develop during the acute rise in the infection, is due to some factor other than phagocytosis. On the other hand the acquired immunity leading to the crisis and recovery is due to active phagocytosis, as this can be interfered with by blockage of the phagocytic cells. He (p. 650) has produced a high degree of immunity in birds by the intravenous injection of vaccines of *P. cathemerium* prepared either by subjecting infected red cells to the action of 1 per cent. formalin, or to a temperature of 50°C. for ten minutes. The immunity is not, however, as great as that which follows natural infection, and depends on the quantity of vaccine administered. A vaccine of normal, uninfected, blood hastens recovery after the crisis, an effect probably due to activation of the lymphoid-macrophage system leading to more intensive phagocytosis than normal.

LUMSDEN and BERTRAM (p. 414) record the results of a study of the biology of *P. gallinaceum*. JACOBI (p. 566) writes of the biology of *P. gallinaceum*; there is no clear-cut cycle of development. Chronically infected birds show marked immunity to superinfection, but birds

clinically recovered may harbour parasites for at least 1½ years. BELTRAN and LARENAS (p. 567), however, state that the schizogony cycle of *P. gallinaceum* occupies 36 to 42 hours and that there is a high degree of synchronicity, with considerable variations from bird to bird.

TERZIAN (p. 567) gives a description of the biological characteristics of *P. lophurae*.

Working with *P. lophurae* in young chicks, TALIAFERRO and TALIAFERRO (p. 714) have shown clearly that acquired immunity can be passively transferred provided that sufficient doses of immune serum are used and continued over a sufficient period.

DAS GUPTA and SIDDONS (p. 715) describe *P. praecox* var. *muniae*, a parasite of the munia ; it is similar to the classical form of *P. praecox* but differs in not being infective for the Indian house sparrow and only slightly for the canary.

LUMSDEN and BERTRAM (p. 414) have investigated the action of plasmoquine and of praequine on gametocytes of *P. gallinaceum*, giving information on the doses required to prevent infection of mosquitoes. There appears to be no difference in action between the two drugs. MANWELL *et al.* (p. 651) report that sulphapyridine is effective against *P. circumflexum* but not against *P. relictum* var. *matutinum* and *P. nucleophilum*. AFRICA *et al.* (p. 415) have obtained success in the treatment of *P. relictum* infections of birds with prontosil.

Charles Wilcocks.

LEPROSY.

ORISSA : ANNUAL PUBLIC HEALTH REPORT FOR YEAR 1939 AND ANNUAL VACCINATION REPORT FOR YEAR 1939–40 [VERGHESE (G.), Director]. pp. 38–43.—**The Annual Report of the Executive Committee of the Provincial Council of the British Empire Leprosy Relief Association (Indian Council), Orissa Branch for the Year 1939–40.**

This report deals with extensive treatment of leprosy cases at the dispensaries and hospitals of the province at a small cost, due to the cordial cooperation of the medical men in charge of these institutions, following on well organized surveys and propaganda by the local Leprosy Association. During 1939–40, 9,625 cases were under treatment as out-patients, doubtless mostly early cases, for 96 per cent. showed some definite improvement after a year's treatment. In addition Village Leprosy Relief Committees have been successful in obtaining voluntary isolation of a number of infective cases in villages or in their own homes as advocated by MUIR. The examination of a population of 822,629 persons in 2,271 villages resulted in the detection of 5,699 cases and 129 more were detected among 14,000 school-children. The number of infectious cases now isolated is 782, an increase of 247 over the previous year. The year's expenditure amounted to £1,544 only among a population of over 7,000,000. *L. Rogers.*

GUINTO (Ricardo S.) & RODRIGUEZ (Jose N.). **A Field Study of Leprosy in Talisay, Cebu, Philippines.**—*Internat. Jl. Leprosy.* Manila. 1941. Apr.–June. Vol. 9. No. 2. pp. 149–166. With 2 figs. & 1 plate.

This is a detailed study of the distribution and incidence of leprosy in the municipality of Talisay in the Cebu Province of the Philippine Islands.

The area includes a coastal, a riverine and a mountain area, in which a house-to-house census and a sanitary and sociological survey were made. The area is economically better off than the previously surveyed Cordova district. About two-thirds of the estimated population was surveyed, including 10,672 persons, 99·3 per cent. of whom were seen. Talisay is one of the most highly infected municipalities of Cebu, from which 403 leprosy cases had been reported since 1903. The registered living lepers numbered 143, of whom 84 were segregated, and 65 more were discovered, bringing the total incidence up to 19·5 per mille inhabitants. Only 11 of the 65 new cases were bacteriologically positive and should have been segregated. Of the total cases in the municipality 36 per cent. were in the quiescent or arrested state, including those paroled. The lowland area showed a rate of 22·5 per mille, the mountain 18·8 and the coastal area 19·5. Wide variations were found in subdistricts, and it appeared that low incidence was due to few cases having been introduced into them. The highest incidence was in the 30–39 age group, but inquiries into the age of onset revealed the highest incidence of 29·8 per cent. in the 10–14 year old group, and 64·9 per cent. from 0–19, 18·3 per cent. from 10–29 and only 16·8 per cent. in later decades. In the Cordova survey 85 per cent. were in the 0–19 group, and 35 per cent. gave a history of house contact with a previous case. In Talisay that figure was 37 per cent., but of 2,072 families only 187 were "leper" families in which one or more fresh cases had developed. There was the same tendency as had been noted in Cordova for most cases to occur where there was overcrowding. A study of water supply and excreta disposal showed no significant differences between leper and non-leper households. Talisay has high hookworm but low yaws incidence. *L. R.*

Guinto (Ricardo S.) & Rodriguez (José N.). **A Leprosy Survey of a Control Area—Santander, Cebu, Philippines. With a Very Low Prevalence of Leprosy.**—*Internat. Jl. Leprosy.* Manila. 1941. July–Sept. Vol. 9. No. 3. pp. 315–325. With 1 fig.

This area of Cebu was selected as having a low leprosy rate. Of a total population of 6,673 as many as 98·6 per cent. were examined, but only two bacteriologically negative cases of leprosy were found in addition to two previously known cases, one of which had been fatal. This gives a rate of 0·45 per mille against 17·6 in Cordova and 19·7 in Talisay, found in the previous surveys. Spread had occurred only within the originally infected household. Except for being a more isolated area, it is difficult to account for the low leprosy rate in Santander, but overcrowding was less than in the other areas.

L. R.

Rai (Schowa). **Leprosy in Canton. A Survey.**—*Taiwan Igakkai Zassi* (*Jl. Med. Assoc. Formosa*). 1941. June. Vol. 40. No. 6. [In Japanese pp. 1133–1162. With 5 figs. & 1 chart. [19 refs.] English summary pp. 1162–1163.]

In the whole of China it has hitherto been thought that there were about one million lepers, with particularly heavy incidence in the Province of Canton. The author has examined 52,000 persons in the city of Canton; these belonged to four groups:—the Tammins, living entirely in boats; the passengers in boats on the river; people

found in the streets; and villagers. Of these, leprosy was found in 84, representing an incidence of 1·6 per 1,000, a rate lower than has been estimated by others. It is pointed out that eczema and scabies are common in Canton, especially in the boat dwellers, and may be mistaken for leprosy. The neural type of disease is more common than the nodular. *C. W.*

Rossas (Thomas Pompeu). **Leprosy in the State of Maranhão, Brazil.** —*Internat. Jl. Leprosy.* Manila. 1941. Apr.–June. Vol. 9. No. 2. pp. 167–176. With 5 figs. on 1 plate.

This is a study of the incidence of leprosy in the Maranhão Province in the north-east of Brazil. The climate is hot and humid in the first six months of the year and dry in the second half. It is mostly low-lying and well watered with a heavy rainfall. The population is very mixed, with much Negro blood, and mostly rural with very bad housing conditions and undernourishment. The disease first appeared in the coast town of St. Louis and spread inland; it has been known to be widely prevalent since 1826. In 1890 the number of cases was estimated at 300, but in 1922–23 1,023 were recorded, 995 of which are analysed. Males, as usual, were about twice as numerous as females, and the largest number fell in the age period of 20–29 years. A recent census in 1939–40 revealed 1,000 cases, or 1·8 per mille; nearly three-fourths of these were reported by travelling doctors. Closed cases formed 61 per cent., and children only 6·1 per cent. All races are equally affected.

In the earlier period two leper asylums and three leper villages were established, but since 1920 modern methods of control have been adopted. A leprosarium-colony has been founded which now provides for 160 patients, but is being enlarged to accommodate 500; the organization is described. Chaulmoogra derivatives are mainly used in treatment. The author advises the appointment of three travelling physicians to re-examine domiciled patients and their contacts and to verify new cases, together with the establishment of treatment posts under male nurses in the principal foci of the disease, to be visited by the physicians, as an economical plan to control the disease in a relatively short period of time. *L. R.*

Reviriego (Antonio J.). Contribución al estudio de la lepra en Entre Ríos. [**Leprosy in Entre Rios.**]—*Semana Méd.* 1941. July 24. Vol. 48. No. 30. pp. 231–235. With 2 figs.

According to Puente in 1938 Entre Rios came sixth among the Argentine provinces as regards prevalence of leprosy. Misiones had 2·433, Formosa 1·509, Corrientes 0·691, Santa Fé 0·639, Chaco 0·489, and Entre Rios 0·353 per thousand inhabitants; by 1940 there were, in the last-named, 364 among a population of 812,645, or 0·423 per mille. Of seventy patients studied, 21 were between 20 and 30 years of age, and 13 between 50 and 60 years. Of these seventy the author states "in 60 per cent. the course was severe and the condition infective; hygienically, the conditions of 78·6 per cent. were bad, medical aid was inadequate in 68 per cent., the economic status of 84·2 per cent. was bad, and the subjects lived together in close contact; a ready soil for propagation of the Mycobacterium leprae." *H. H. S.*

Pesce (Hugo). Apuntes para la geografía de la lepra en la Sierra del Perú. [**Distribution of Leprosy in Peru.**]—*Actualidad Med. Peruana.* Lima. 1941. May. Vol. 7. No. 1. pp. 8–12. [17 refs.]

Cot Lesmes (Vicente). La lepra en Santiago de Cuba. (Reporte de 105 casos.) [**Leprosy in Santiago de Cuba.**]—*Rev. Méd.-Quirúrg. de Oriente.* Santiago de Cuba. 1941. Sept. Vol. 2. No. 3. pp. 168–171.

In the 9 months, May 1939–January 1940, the author reported on 30 cases of leprosy which he had seen and he stated that since several of these presented open and infectious lesions, the incidence was likely to go up. Between February 1940 and May 1941 he has seen another 75 cases and he now comments on the total 105. Forty-two were of the nodular type, 50 of the neural and 13 mixed, or 40, 47·6, and 12·4 per cent. respectively. Sixty-one were females, 44 were males. As regards age, none was under 5 years, 7 (6·6 per cent.) were between 5 and 10 years, 16 (15·2) between 10 and 15 years, 14 (13·3) between 15 and 20 years, 33 (31·4) between 20 and 30 years, and in succeeding decades 13 (12·4), 9 (8·6), 8 (7·6) and over 60 years 5 (4·8). He estimates that there are " 2,000 to 4,000 lepers in Cuba " [a wide margin]. It is far from uncommon to find more than one affected in a family, and the disease would seem to cause little fear since lepers were found in such occupations as hairdressers, cooks, a restaurant chef, butler, servant-maids, dressmakers, laundresses, tobacconist, tramway conductor, students, etc. *H. H. S.*

Doull (James A.), Rivera (E. Martinez), Saunders (George M.), Guinto (Ricardo S.) & Morales (E. Garrido). **A Note on Leprosy in Puerto Rico.**—*Bol. Asoc. Med. de Puerto Rico.* 1941. June. Vol. 33. No. 6. pp. 217–223.

This note deals with the history and present incidence of leprosy in Porto Rico. The disease is believed to have been introduced in the early days of the slave trade, and was looked on with indifference until, about 1870, a few cases were hospitalized. Since 1912 the recorded deaths from leprosy averaged 4·5 annually. In 1940 the known cases numbered 102, but at least as many more are believed to exist. The examination of 1,873 schoolchildren revealed no cases, so the problem does not appear to be a serious one. *L. R.*

Aycock (W. Lloyd) & Hawkins (James W.). **Regional, Racial, and Familial Relationships in Leprosy in the United States.**—*Public Health Rep.* 1941. June 27. Vol. 56. No. 26. pp. 1324–1336. With 4 figs.

The data in this paper are based on information concerning 927 admissions to the Carville settlement. Foreign-born leprosy patients numbered 430, introduced by immigration from fourteen countries. The American-born numbered 497, of whom 370 belonged to southern States of California, Texas, Louisiana and Florida. Out of 396 stationary patients only 4 failed to give history of contact with a local or foreign focus of leprosy and 491 of 497 native-born persons can be allocated to known areas of prevalence of the disease. In Texas there is a concentration of cases of German stock. *L. R.*

HANKS (John H.). **Behavior of Leprosy Bacilli in Complex Liquid Media with Highly Available Sources of Nutrient and Accessory Substances.**—*Internat. Jl. Leprosy.* Manila. 1941. July–Sept. Vol. 9. No. 3. pp. 275–298. [28 refs.]

This is an account of a further painstaking attempt to cultivate the bacillus of Hansen. The author assumes that some of the bacilli in lepromatous lesions are living and consequently it is necessary to study a variety of physiological conditions which might make it possible to cultivate the bacilli from each lesion. The media were prepared on the principle that highly pathogenic bacilli are deficient in the power to synthesize enzymes and other materials required for the production of new cells. Blood and serum were used, supplemented by a variety of combinations of digestion or extraction products of blood, egg yolk, tissues, acid-fast bacilli and yeast, also with peptones, Long's synthetic medium, and other simple sources of nitrogen and carbon. Further, tissue extracts, sterile egg-yolk suspensions, and chick embryo juice were used as basic solutions, supplemented in similar ways. Liquid media were used, with blood and Long's medium as the basis, as liquid media permitted estimates to be made of the number of bacilli present from time to time to provide badly needed quantitative methods to allow the fate of the inoculated bacilli to be followed. Finely ground suspensions of subcutaneous lepromatous nodules were used for inoculating media. The original paper should be consulted regarding the technique, which is fully described. Fifteen nodules were used after the rejection of two. A number of the tubes were incubated under partial pressures of CO_2.

Diphtheroid bacilli were most frequently grown, but three of the six cases furnishing them showed ulcers of the skin, so they are considered to be contaminations. In addition one of the ulcerated cases yielded cultures of one streptothrix and two acid-fast bacilli only in single inoculated tubes, the latter being dissimilar; these also are not regarded as the causative organisms of leprosy. One non-ulcerated case also yielded an acid-fast bacillus which is not considered to be different from those obtained by earlier workers, nor were they tubercle bacilli. Moreover, quantitative microscopical examinations of the liquid media at intervals revealed no evidence of multiplication of the inoculated leprosy bacilli in any of the 109 nutritional combinations tested. Nor did growth take place in media shown to be suitable for the cultivation of human blood monocytes or of the fibroblast of the lepromata. This well-planned attempt to cultivate the leprosy bacillus on scientific lines has, therefore, so far yielded negative results. *L. R.*

DHARMENDRA. **Complement-Fixation by Leprous Sera after Absorption by Various Acid-Fast Bacilli.**—*Indian Jl. Med. Res.* 1941. July. Vol. 29. No. 3. pp. 523–525.

This note deals with the complement-fixing power of leprous sera before and after absorption with different acid-fast bacilli. Absorption of the sera was carried out by mixing them with thick bacillary suspensions, allowing the mixture to stand overnight, and then filtering through a candle. The bacilli of Lleras, Duval, Bayon, *Myco. phlei* and one from a leprous nodule were used. An unabsorbed portion of the serum and portions absorbed by each of the five bacilli were tested for their complement-fixing power in the presence of all of six antigens

[four from leprous material, one from *Myco. tuberculosis*, one from *Myco. phlei*] in dilutions of from 1–5 up to 1–200, sera from twelve lepromatous cases being used. In dilutions of 1–25 and upwards the complement-fixing power of the absorbed sera was less than that of the unabsorbed, all the bacillary emulsions acting in a similar manner. Control staphylococcus cultures gave variable results. The author concludes that the experiments afford no proof of the specificity of any of the bacilli and that such complement-fixation tests are unlikely to furnish any evidence for or against the genuineness of such acid-fast cultures. *L. R.*

DE SOUZA-ARAUJO (H. C.). **Pathogenicity of Acid-Fast Bacilli Isolated from Human Leprosy by Migone.**—*Internat. Jl. Leprosy.* Manila. 1941. Apr.–June. Vol. 9. No. 2. pp. 209–214. With 7 figs. on 2 plates.

The author reports animal inoculations with two new strains of acid-fast bacilli isolated from skin lesions of human leprosy by MIGONE in Paraguay. The injection of these cultures into rats and mice produced typical granulomata similar to those obtained with emulsions of human leprous nodules. They affected the skin and muscles, and so differed from infections with Stéfansky's rat leprosy bacillus. The granulomata were rich in globies (clusters) of acid-fast bacilli, which are seldom obtained in experiments with cultures. *L. R.*

CHAUSSINAND (R.). Contributions à l'étude de la lèpre. II. Inoculation du bacille de Hansen au singe. [**Inoculation of Human Leprosy Bacilli into the Monkey.**]—*Internat. Jl. Leprosy.* Manila. 1941. Apr.–June. Vol. 9. No. 2. pp. 203–208. With 1 plate.

These experiments were carried out on *Macacus cynomolgus* with an emulsion rich in lepra bacilli and by various routes. Nodules of various sizes resulted in from three to five weeks, and they were reabsorbed without leaving any trace at the end of about one and a half months. The reappearance of the vanished first nodules may occur after a fresh inoculation of lepra bacilli in another part of the body, but after several inoculations they re-form and disappear again more rapidly than before ; the nodules do not reappear after a fourth reinoculation. Immunization is thus gradually brought about. These monkeys are therefore not absolutely refractory to human leprosy. *L. R.*

FITE (G. L.). **Development of a Leprous Process in Rats at the Site of Inoculation with Material from Human Leprosy.**—*Public Health Rep.* 1941. Sept. 26. Vol. 56. No. 39. pp. 1919–1922.

The author records that 6 out of 154 rats inoculated with emulsions of human leprosy nodules developed, after an incubation period of about 18 months, nodules at the site of the inoculation resembling those of rat leprosy, but in which the bacilli tended steadily to decrease. Mucin suspensions of the inoculated material gave a much larger proportion of positive results with more numerous bacilli. *L. R.*

Nolasco (J. O.) & Lara (C. B.). **Histological Study of an Early Case of Leprosy in a Young Child of Leprous Parents. Report of a Case, with Autopsy.**—*Internat. Jl. Leprosy.* Manila. 1941. Apr.–June. Vol. 9. No. 2. pp. 181–192. With 1 fig. & 2 plates. [18 refs.]

This is a full report on the histological findings in an early infection in a child who died from pneumococcal empyema when 17 months old. Two months previously a weal-like lesion, containing numerous lepra bacilli, had been detected on the right knee, which was regarded as a primary lesion, but two days before death only a slightly depressed non-indurated scar remained. This was found histologically to be a very young leproma with numerous bacilli and some foamy cells. Lepra bacilli were also found in considerable numbers in the corresponding lymphatic nodes of the part, but not elsewhere in the lymph nodes, nerves or other organs. This indicates spread from the primary lesion through the lymphatic channels. Two plates illustrate the histology of the lesions. *L. R.*

Campos (Nelson Souza) & Ribeiro (Eurico Branco). Nevrite e caseose de nervo na lepra tuberculoide. [**Neuritis and Caseation of Nerves in Tuberculoid Leprosy.**]—*Ann. Paulist. Med. e Cirurg.* 1941. June. Vol. 41. No. 6. pp. 527–529.

A child of five years of age was apparently healthy till the age of four years. She then developed a small reddish nodule, the size of a pin's head with a pale surround in the right temporal region. This disappeared with treatment, leaving a scar. A few months later a thickening of the ulnar nerve of the right arm was noticed, but caused no pain. Mitsuda reaction was +++, but no bacilli were found and there was wasting of the muscles of the hand. Some 18 months or so after this, operation was undertaken and creamy pus was found coming from the nerve.

The author states that caseation, which is the last stage in the tuberculoid process, starts always in the centre of the nerve, extends axially, destroying the central fibres, forming necrotic foci at short intervals, then passing, hernia-like, through the epineurium, forming small swellings along these nerves of small calibre, and pedunculated swellings in the trunks of the larger nerves. According to their intensity they remain deep or open to the exterior. In the latter case, cicatrization occurs with adhesion of the skin to the nerve below and the formation of a characteristic retractile scar. *H. H. S.*

Stein (A. A.) & Wyschnewsky (A. A.). Ein Fall von Lepra mit kaseoesen Veraenderungen in den Nerven. [**Leprosy with Caseous Changes in the Nerves.**]—*Internat. Jl. Leprosy.* Manila, 1941. July–Sept. Vol. 9. No. 3. pp. 305–308. With 4 figs. on 1 plate.

This is a report on the microscopical changes in two nodules removed from a nerve in a case of anaesthetic leprosy. The patient showed thickening and nodulation of the left ulnar, and to a less extent of the median nerve, accompanied by anaesthesia and partial claw hand, but no skin lesions. Microscopical examinations were made of two nodules the size of a pea with the following results. In the centre necrosis was found, around which were seen epithelioid and giant cells, surrounded

by a ring of lymphocytes. Around the whole was a fibrous layer, the only vascular part of the nodule; the whole was diagnosed as neuro-fibromatous. The lesions were, therefore, tuberculoid in nature. *L. R.*

FITE (G. L.). **The Vascular Lesions of Leprosy.**—*Internat. Jl. Leprosy.* Manila. 1941. Apr.–June. Vol. 9. No. 2. pp. 193–202. With 27 figs. on 6 plates. [13 refs.]

The author reports on a study of the vascular lesions of leprosy, based on 77 cases and 10 autopsies, and illustrates his paper with six plates showing the microscopical appearances. In the case of the larger vessels the endothelial cells of both arteries and veins showed diffuse infection with lepra bacilli, apparently resulting from spread in the endothelium. In the small arteries only, large groups of bacilli were found in the smooth muscle cells. In the larger vessels the infection seemed to be spreading through the vasa vasorum especially in the subcutaneous plexus. Lepromatous thickening of a large vein and a mass projecting into the lumen of an artery were each found once. Tuberculoid changes in a large vein were also seen. Vascular involvement of the testis and of the nasal mucosa were also noted, but not of the peripheral nerves or the lymph nodes. Leprosy foci apparently originate in the perivascular lymph spaces around arteries, veins and nerves, but were not demonstrated in the lymphatic vessels themselves. It is probable that the bacilli are discharged from the endothelial cells into the circulation continually in lepromatous cases. Bacilli were also demonstrated in the liver and spleen. *L. R.*

VENKATASUBRAMANIAM (C. S.). **Investigations on the Biochemistry of Leprosy (Part I).**—*Leprosy in India.* 1941. July. Vol. 13. No. 3. pp. 104–108.

In this note the author records observations to show that in leprosy cases both calcium and phosphorus in the blood are within normal limits, but phosphatase shows a definite but slight increase, which is attributed to the bone changes. This is confirmed by a note by the editor pointing out that the phosphatase increase shows a higher average in the nerve than in the lepromatous type of case. A slight reduction in the total protein may be due to malnutrition. *L. R.*

WADE (H. W.). **Heredity in Susceptibility to Leprosy.** [Editorial.]—*Internat. Jl. Leprosy.* Manila. 1941. July–Sept. Vol. 9. No. 3. pp. 353–358. [10 refs.]

This is an instructive review of the recent literature on this subject. The suggestion of MOLESWORTH that the Middle Ages decrease of leprosy was due to the elimination of susceptibles was controverted by MUIR. AYCOCK in America regarded the family occurrence of the disease as evidence of hereditary predisposition. Muir found Europeans to be susceptible, but found the disease more severe in Burmans. LOWE considers that inherent individual susceptibility is an important factor. COCHRANE regards close contact as by far the most important factor in infection. READ inclines to regard acquired constitutional weakness and malnutrition as of importance. Wade thinks that only

experimental investigations on animals susceptible to leprosy can afford definite evidence on the subject. Skin reactions to injections of leprosy bacilli might aid. *L. R.*

FONTE (Joir). A lepra no Hawaii. Quinze anos de atividade do centro de leprologia de Honolulu (Hawaii)—(1925–1939). [**Leprosy in Hawaii. Fifteen Years of Investigations at the Honolulu Centre.**]—*Acta Med.* Rio de Janeiro. 1941. June. Vol. 7. No. 6. pp. 289–297. English summary (4 lines).

Several lines of study have been undertaken but the information given in this article is too brief and sketchy to have much value ; few details are given. The subjects studied include : (1) Glycosuria in lepers. Of 175 patients 23 per cent. were excreting sugar, whereas of 300 others examined by way of control, only a little over 3 per cent. had glycosuria. (2) Blood protein in lepers ; certain results have been observed but they have not yet been analysed. (3) Cytology of the blood. Exacerbations of the disease, acute or subacute, are preceded by leucocytosis, [polymorphonuclears] relative and absolute ; regression of the lesions by reduction of these and increase of large mononuclears ; in convalescence both are reduced with corresponding increase of small lymphocytes. (4) Sedimentation rate of red corpuscles ; nothing definite has resulted from this investigation into the rate of sedimentation and the clinical course of the disease. (5) The Wassermann reaction. Dr. BADGER found that 29 per cent. of the patients reacted positively, but among 481 controls in whom repeated examination failed to reveal clinical signs of syphilis 29·6 per cent. gave a positive, while only a few more, 32·6 per cent., were positive among 834 patients attending the venereal clinic. Hence the author concludes that the Wassermann (or Kahn) reaction is of little value in differentiating leprosy from syphilis. The rest of the article deals briefly with epidemiological matters. *H. H. S.*

FONTE (Joir). A lepra no Hawaii. Quinze anos de atividade do centro de leprologia de Honolulu (Hawaii)—(1925–1939). [**Leprosy in Hawaii.**]—*Acta Med.* Rio de Janeiro. 1941. July & Aug. Vol. 8. Nos. 1 & 2. pp. 28–44 ; 73–86. English summaries (8 lines).

In this third contribution the author sketches the bacteriology and treatment of the disease by chaulmoogra, artificial pyrexia, cod liver oil, carbonic acid snow, iodides and arsenicals ; and in the fourth he deals with general therapeutic measures and the treatment of special symptoms and complications such as neuritis, perforating ulcer, ocular and nasal lesions. A final section deals with murine leprosy, but contains nothing not already known to readers of this *Bulletin.*

H. H. S.

ARNOLD (Harry L.), Jr. **Differential Diagnosis in Leprosy.**—*Arch. Dermat. & Syph.* 1941. Nov. Vol. 44. No. 5. pp. 911–912.

Negative results to examinations of nasal smears or to tests of sensitivity to light touch or pinprick are not enough to exclude leprosy. The principal diagnostic criteria are :—Almost any form of skin lesion—or none at all ; thermal anaesthesia, even in apparently normal

skin ; muscular weakness or paralysis, most easily noted in the facial muscles ; irregularly thickened nerve trunks ; acid-fast bacilli in smears from skin or scraped nasal septum ; histological changes. Of these criteria the most important is thermal anaesthesia, which is almost invariably present in leprosy—this is by no means true of anaesthesia to light touch or to pinprick. Thermal anaesthesia can easily be tested by hot and cold test tubes. In leprosy, as in other diseases, bacterioscopic examinations are valuable when positive but inconclusive when negative. *C. W.*

Schujman (Salomon). Sarcoides dermicos, hipodermicos e intramusculares de origen leproso. [**Sarcoid Lesions of Leprous Origin.**]—*Rev. Argentina de Dermatosifilologia.* 1941. Vol. 25. Pt. 3. pp. 447–460. With 10 figs. English summary.

" A case of leprosy is described in which cutaneous, subcutaneous and intramuscular sarcoid lesions were found. Its leprous aetiology was established by the anaesthetic changes of the skin and nasal mucosal lesions ; by the histopathological examination which showed characteristic leprous neuritis and by the improvement observed with chaulmoogra treatment.

" The typical changes of the lymph nodes, lungs and bones described in Schaumann-Besnier-Boeck disease were not observed in this case.

" The author maintains that this case shows that cutaneous and subcutaneous sarcoids can coexist ; therefore their separation is not always justified. Also that cutaneous sarcoids may exist without the lesions in bone, lymph nodes and lungs described in the Besnier-Boeck-Schaumann disease."

Escalona (Ernesto). La reacción leprosa. [**The Leprosy Reaction.**]—*Medicina.* Mexico. 1941. Aug. 25. Vol. 21. No. 394. pp. 365–377.

Wenger (Franz). **Leprosy with Widespread Tumor-like Tuberculosis.**—*Arch. Pathology.* 1941. July. Vol. 32. No. 1. pp. 112–116. With 1 fig.

This is a brief illustrated account of an unusual case of lepromatous disease in an Indian aged 44, who died after suffering from cough and aphonia. At an autopsy typical dermal and the respiratory tract leprosy was found together with very large tuberculous lesions in the liver and spleen, but the variety of tubercle bacillus was not ascertained. The author advises the use of Sudan III for staining the leprosy bacilli. *L. R.*

Greval (S. D. S.), Das (B. C.) & Sen Gupta (P. C.). **Preparation and Use of the Witebsky, Klingenstein and Kuhn (W. K. K.) Antigen.**—*Indian Jl. Med. Res.* 1941. July. Vol. 29. No. 3. pp. 527–530.

Owing to Witebsky, Klingenstein and Kuhn antigen being no longer obtainable from Europe the authors describe as follows the methods by which they have made a reliable preparation. It consists of a solution in benzol of (1) the alcohol insoluble, (2) the pyridin soluble and, (3) the acetone insoluble fractions of the human tubercle bacillus. In making it the authors took 12 cultures, from six cases of tuberculosis, grown for two months and autoclaved for half an hour in 50 cc. saline,

and dried the filtrate to weight 9·078 grammes. After extraction in 20 times its weight of alcohol, filtering off and drying the bacilli, the remaining weight of 0·788 gramme was extracted in a 50 cc. Soxhlet apparatus with pyridin for 5 hours over a glycerine bath at 130°C. The pyridin solution was removed by distillation and a dried residue weighing 0·1652 gramme of the alcohol insoluble and pyridine soluble fraction was obtained. After extracting this residue with 20 cc. acetone the filtrate was washed with 3 cc. fresh acetone and dried to yield 0·075 gramme of residue, which was finally dissolved in 7·5 cc. benzol and made up to a 1 per cent. solution. As it was milky, 15 cc. of benzol was added in 5 cc. quantities to obtain a clear solution, and one part of 1 per cent. alcoholic solution of lecithin added to two parts of the benzol solution to make the required antigen. In the complement-fixation test for leprosy and kala azar, complement of optimum reaction and titre only, as determined by the Wassermann reaction, is now used by the authors. *L. R.*

Patrick (D. W.) & Wolfe (D. M.). **Leprosy: Complement Fixation with Gaehtgens' Spirochete Antigen compared with Standard Wassermann and Kahn Tests.**—*Public Health Rep.* 1941. Aug. 29. Vol. 56. No. 35. pp. 1757–1759.

The authors have examined the statement of Capelli that complement fixation tests in leprous patients with the use of Gaehtgen's phenolized cultures of *Spirochaeta pallida* (palligen) give no positive 4 or 3 plus reactions in non-syphilitic patients, in contrast to those obtained with the Wassermann method. They conclude that lepers do show a tendency to falsely positive results with Gaehtgen's antigen, although to a lesser degree than with Wassermann and Kahn tests. *L. R.*

Dharmendra & Jaikaria (S. S.). **Studies of the Lepromin Test. (2) Results of the Test in Healthy Persons in Endemic and Non-Endemic Areas.**—*Leprosy in India.* 1941. Apr. Vol. 13. No. 2. pp. 40–47. With 2 graphs.

The authors report on the reactions to the lepromin test in healthy subjects in endemic and non-endemic areas respectively. The endemic area was a highly infected part of West Bengal with an incidence of over 4 per cent. The non-endemic area was in the Punjab where a survey had not revealed a single case of leprosy. The readings were made weekly for six weeks. Tests in 296 healthy persons in the endemic area gave positive reactions in 59 per cent. with increasing incidence at higher ages until 100 per cent. was reached. In the Punjab non-endemic area only 36 per cent. of positive reactions were met with; a rise was noted up to 30 years of age, followed by a decrease. In the Bengal endemic area 22 per cent. of the positive reactions were followed by ulceration, but not in any of the endemic area people. Tuberculin tests by the Mantoux method were also carried out; these showed increased positive reactions with increasing age, and except up to five years of age they were more frequently positive than the lepromin reactions. The authors therefore consider the lepromin test to be one of non-specific allergy, and the findings are not incompatible with the theory that increased positive reactions with increasing age are dependent on the resistance of the tissues,

although they do not prove it to be so. Exposure to infection, as well as increasing age, are factors in increasing the number of positive reactions. *L. R.*

DHARMENDRA. **Studies of the Lepromin Test. (3) Preparation and Standardisation of Lepromin.**—*Leprosy in India.* 1941. July. Vol. 13. No. 3. pp. 77–80.

The author describes a method of separating leprosy bacilli from tissues and nodules and of standardizing the bacillary content. Nodules from the ear lobes were autoclaved, ground in a pestle and mortar with carbol saline and the supernatant fluid after settlement repeatedly centrifuged to remove tissue cells. The bacilli in the collected supernatant fluid were counted and the fluid was diluted to leave 15 million bacilli per cc. The injection of 0·1 cc. of the resulting lepromin gave good results. *L. R.*

FERNANDEZ (Jose M. M.) & OLMOS CASTRO (Norberto). Estandardización de la lepromina. [**The Standardization of Lepromin.**]—*Rev. Argentina de Dermatosifilologia.* 1941. Vol. 25. Pt. 3. pp. 435–446. With 9 figs. [13 refs.] English summary.

"A new method for preparing lepromin based on the different densities of M.L. [*Myco. leprae*] and tissues contained in ordinary lepromin has been developed, which has the advantage of permitting the obtaining of a pure suspension of bacilli and accurate standardization.

"A watery suspension of ground lepromata was given a density of 1·050 with sodium chloride and then centrifuged; the majority of the bacilli remained suspended in the fluid while the cells were precipitated. Alcohol was then added to the separated fluid adjusting it to a density of 0·950; centrifugation precipitated the majority of the bacilli. This sediment was dried in a vacuum and ground to a fine powder. A 1 per cent. suspension was prepared by weighing the appropriate amount and then dilutions of 1 : 10, 1 : 100 and 1 : 1000 were made.

"This preparation, called 'bacillary lepromin,' produced positive reactions in allergic cases and negative reactions in anergic ones. Comparative tests made with different batches of bacillary lepromin and Muir's and Hayashi's lepromin gave similar reactions; those of the bacillary lepromin being of more uniform intensity. A direct relation between the concentration of the bacillary lepromin injected and the intensity of the skin reaction was observed."

LOWE (John) & DHARMENDRA. **Studies of the Lepromin Test. (4) The Early Reaction to Lepromin, its Nature and its Relation to the Classical Mitsuda Reaction.**—*Leprosy in India.* 1941. July. Vol. 13. No. 3. pp. 81–88. [11 refs.]

The authors have studied the relations of early and late reactions to lepromin prepared as described above. They concur in the earlier finding of FERNANDEZ that cases giving the typical late reaction after three to four weeks also gave an early reaction of a less marked nature. Thus among 300 tests 85 per cent. gave both early and late reactions and in only 6·7 per cent. did the early and late reactions differ. The

early reaction is characterized by erythema half an inch or more in diameter, accompanied by an appreciable degree of oedema and thickening of the skin of the whole area. They proceeded to carry out tests with their lepromin after breaking down the bacillary content by grinding, and found the early local reaction to be accelerated from 84 to 24 hours and to be increased in extent, and the degrees of the late lepromin reaction to be considerably diminished. They therefore disagree with Fernandez's suggestion that lepromin contains two antigens, responsible respectively for the early and late reactions; they regard the late reaction as being due to the gradual breaking up of the lepra bacilli at the seat of injection, and the early one to the same antigen set free from the bacilli by grinding, and to be of an allergic nature. Positive results have also been obtained in healthy non-contacts. *L. R.*

DHARMENDRA. **Studies of the Lepromin Test. (5) The Active Principle of Lepromin is a Protein Antigen of the Bacillus.**—*Leprosy in India.* 1941. July. Vol. 13. No. 3. pp. 89–103. [13 refs.]

This paper records promising results regarding the fractionation of lepromin in order to obtain the antigen in a soluble form. The conclusion reached, that the antigen of lepromin is contained solely in the lepra bacilli, and not in the tissues of a nodule, and that it can be obtained in a soluble form by breaking up the separated lepra bacilli to produce an early local reaction on injection, led to attempts to fractionate the dried bacillary powder separated from leprous nodules. These observations led to the conclusions: (1) that no isolated fraction gives a late reaction, (2) that only the protein content, and not the lipoid fractions, gives rise to a definite early reaction. A comparison between the late reactions with ordinary lepromin, and early ones with the ground-up material, gave agreement in 88·8 per cent. of 90 cases. The early reaction with a pure antigen is easy to perform and to read and is as sensitive as the former test without the disadvantage of a long wait and undesirable late reactions. *L. R.*

RUDOLF (Elmar). Beitrag zur Frage der Rubinoreaktion. [**Rubino Reaction.**]—*Deut. Tropenmed. Ztschr.* 1941. Aug. 15. Vol. 45. No. 16. pp. 496–505. [50 refs.]

After discussing the nature and technique of the Rubino reaction, the author summarizes in tables the results obtained by various observers and arrives at the following conclusions. The Rubino reaction is specific in the diagnosis of leprosy. It only gives an insignificant number of positive reactions in control non-leprosy cases, namely 0·98 per cent. among 14,050 collected data. Of 1,551 cases of leprosy of all forms combined positive reactions were obtained in 67·5 per cent. In the different forms, among 702 cases, nodular leprosy gave 71·3 per cent., mixed 71·7, nerve 33·0, and maculo-anaesthetic 19·8. For its use in the diagnosis of doubtful suspected cases of leprosy the evidence as yet is inconclusive. Tuberculosis gives no specific results with the test. The reaction is a distinct one, and unrelated to the sedimentation, Wassermann and flocculation tests for syphilis. Generally speaking it suffices to perform the test with one small tube. [See also this *Bulletin*, 1939, Vol. 36, pp. 691, 933.] *L. R.*

British Empire Leprosy Relief Association. Madras Provincial Council. **Annual Report 1940–41.**—37 pp. Printed at the Arpudha Press, Chingleput.

This report presents the following points of interest in addition to those of only local importance. A further trial of skimmed milk in the diet of lepromatous patients has not confirmed the very favourable conclusions from a former trial, but the observations are being continued. Further trials of adding the rather unpalatable ragi to wheat in a diet indicate that it may be of some value in relieving chronic nerve and bone pain. A trial of M. & B. 693 [sulphapyridine] showed that it is liable to produce severe and injurious febrile reactions without being followed by any benefits; so this drug is definitely contraindicated in leprosy. A non-irritating ethyl ester of chaulmoogric acid supplied by Cole from S. America was well tolerated and promising as far as limited trials indicate. The Siam diphtheria antitoxin and formol toxoid treatment did not confirm the claims of its originators. Further work on childhood leprosy indicates that the percentage of negative lepromin tests increases with the degree of the exposure of the children to family contact with infective cases of leprosy. *L. R.*

Cole (Howard Irving) & Cardoso (Humberto T.). **Analysis of Chaulmoogra Oils.**—*Internat. Jl. Leprosy.* Manila. 1941. Apr.–June. Vol. 9. No. 2. pp. 215–228.

This is an important paper recording the first quantitative analysis of the chaulmoogra oils *Hydnocarpus wightiana, H. anthelmintica* and *Taraktogenos kurzii,* so much used in the treatment of leprosy. The most important earlier work was that of Power & Gornal and Power & Barrowcliff in 1904 and 1905, since which little has been done. The following table, constructed by combining two tables in the paper, shows the main points.

Percentage composition of the fatty acids of chaulmoogra oils.

	H. wightiana	*H. anthelmintica*	*Taraktogenos kurzii*
Hydnocarpic	48·7	67·8	34·9
Chaulmoogric...	27·0	8·7	22·5
Gorlic	12·2	1·4	22·6
Oleic	6·5	12·3	14·6
Palmitic	1·8	7·5	4·0
Lower homologues of chaulmoogric acid	3·4	0·1	0·4
Loss	0·4	2·2	1·0

Analysis also showed that *H. wightiana* oil is quite similar in composition to that of the Brazilian *Carpotroche braziliensis* oil.

The authors point out that if gorlic acid should prove the most effective fraction of the oil in the treatment of leprosy, then the oil of *Taraktogenos kurzii* may be the most effective, although the difficulty of obtaining it pure from the Burma forest during the rainy season led to the preference for the hydnocarpus oils. However, they obtained

pure oil from the Burma trees successfully grown in Brazil and found it to keep well. On the other hand, if the hydnocarpus fraction is the most effective (as ROGERS found it to be in Calcutta) then the hydnocarpus oils will be the best, especially the *H. anthelmintica* of Indo-China, if still obtainable.

From the chemical point of view the most interesting part of this highly technical paper relates to the fraction shown in the table as the lower homologues of chaulmoogric acid, for although forming but a small part of the oils, no less than five new substances have been found, four of which have been isolated and described under the names of alepric, aleprylic, aleprestic and aleprolic acids. The first two have melting points of 48° and 32°C. respectively, which are lower than those of chaulmoogric and hydnocarpic acid. Owing to the great difficulty of isolating them in any considerable amounts they appear to be of more theoretical than practical value. *L. R.*

CHAUSSINAND (R.) in collaboration with J. GUILLERM. Contributions à l'étude de la lèpre. III. Traitement de la lèpre humaine par le " Krabao " (*Hydnocarpus anthelmintica* Pierre). [**Treatment of Human Leprosy with** *H. anthelmintica* **Oil.**]—*Internat. Jl. Leprosy*. Manila. 1941. July–Sept. Vol. 9. No. 3. pp. 327–340. With 10 figs. on 2 plates. [14 refs.]

The authors describe the results of their treatment of 375 cases of leprosy with various preparations of *Hydnocarpus anthelmintica* oil, locally known as Krabao, and give photographs of cases. At dispensaries out-patients were treated by the sodium soap made from the oil, orally in doses of six tablets of 25 cgm. each three times a day, which were well tolerated and as effective as larger doses. This form of treatment can be continued for years with intervals of a few weeks. It proved to be of value, especially in early cases, and popular with the patients. The authors also think it should be of great value in the prophylactic treatment of children living in contact with leprosy patients. In more advanced cases it seldom clears up the lesions. In patients requiring more active treatment they prefer the ethyl esters, undistilled and unneutralized, prepared by cold extraction from the oil. These have been given intradermally, intravenously, intra-arterially, intramuscularly and subcutaneously, with intramuscular injection for choice. Remarkable results have been obtained in out-patients at little cost. In Cochin China the segregation laws are not applied severely and they have not resulted in any appreciable results in reducing the disease, but cause hiding of cases inimical to dispensary treatment and prophylaxis. Dispensary treatment is therefore recommended, combined with rigorous segregation of those who refuse treatment and are a danger to the community. [See this *Bulletin*, 1940, Vol. 37, p. 634.] *L. R.*

EMERSON (G. A.). **Some Pharmacologic Effects of the Choline Ester of Chaulmoogric Acid.**—*Internat. Jl. Leprosy*. Manila. 1941. July–Sept. Vol. 9. No. 3. pp. 341–345. With 1 fig.

The authors report on the pharmacology of one of the many chaulmoogra derivatives, prepared by WRENSHALL in Hawaii, namely chaulmoogrylcholine, or the chaulmoogric acid ester of choline. Their results bear out the importance of their view regarding the necessity

to ascertain the toxicity and physiological actions of a new preparation before using it clinically, for its chloride proved to be too toxic for human use in significant amounts. Thus it has a depressor effect on the circulation, not completely antagonized by atropine, and on muscular action. It also has a high haemolytic activity and a harmful effect on tissues. It is not therefore suitable for trial in leprosy cases.

L. R.

COLLIER (D. R.). **The Effects of Diphtheria Toxoid on Painful Enlarged Nerves in Leprosy.**—*Internat. Jl. Leprosy.* Manila. 1941. Apr.–June. Vol. 9. No. 2. pp. 177–180.

This brief note records four cases in which the administration of diphtheria toxoid was followed by relief of the pains in cases of enlarged nerves of leprosy. Previously operations on such painful nerves had only given temporary relief on account of the formation of scar tissue. It is stated that the new treatment has given satisfactory results in more than 300 cases. Temporary hot and itching sensations and increased pain in the hands and feet may occur after the injections.

L. R.

MCKEAN (J. Hugh). **Limitations of the Diphtheria Toxoid Treatment of Leprosy.**—*Internat. Jl. Leprosy.* Manila. 1941. July–Sept. Vol. 9. No. 3. pp. 309–314.

——. **Limitations of Toxoid Treatment.** [Correspondence.]—*Ibid.* p. 359.

The author records his experience of the diphtheria toxoid treatment of leprosy at the Chiengmai Leper Asylum during 18 months. He states that the limitations of the treatment were evident from the beginning, and he quotes the statement of COLLIER in his third report that the response to the treatment was not uniform. Indeed, wide variations were noted in the same class of cases. The best results were seen in tuberculoid cases with few bacilli and in early neural cases, just those that do best under chaulmoogra treatment. The earlier lepromatous cases (L1) showed excellent results at first, but 3 of 21 relapsed, so the permanence of the improvement in the others requires further observation. The treatment proved to be of no value in either major tuberculoids with numerous bacilli, or in the papular type of lepromatous cases, and even active minor tuberculoids free from bacilli failed to respond. In early favourable cases the results appear quickly. In cases which relapse, further treatment is of little use, and new activity tends to appear in other parts of the body. In only 38 of 286 cases was unusually great fragmentation of bacilli noted.

[In connexion with the failures of several experienced workers to confirm the beneficial results of diphtheria toxoid treatment claimed by the Thailand workers it may be well to call attention to a leading article on the subject in the *Internat. Jl. Leprosy*, 1941, Vol. 9, p. 229. In this it is pointed out that not since the first trial of the aniline dyes has so much been claimed for a therapeutic innovation as in the case of diphtheria toxoid by the Thailand workers. The hypothesis of adrenal deficiency in leprosy on which its use is based, together with the assertion of OBERDOERFFER that the consumption of Colocasia predisposes to leprosy, still lacks any reliable basis, consequently " as yet, indeed, there can be seen no justification for employing this

treatment on any other than an experimental basis." An addendum to this editorial expresses regret that an article entitled " New hope for the Leper " has appeared in a popular American magazine illustrated by a posed photograph of Dr. Collier. See also this *Bulletin*, 1941, Vol. 38, pp. 26, 704.] *L. R.*

DAVISON (A. R.) & GRASSET (E.). **Diphtheria Toxoid in the Treatment of Leprosy. Clinical and Immunological Investigations.**—*Leprosy Review*. 1941. Oct. Vol. 12. No. 4. pp. 68–79.

This is a careful record of a trial of diphtheria formol toxoid in South Africa by experienced workers. One hundred cases were treated with doses of 0·5 cc. increased to 10 cc. over a period of seven months, in accordance with the suggestions of COLLIER of Thailand, and the results were assessed nine months from the beginning. The diphtheria formol toxoid used was prepared in the South African Institute for Medical Research. In 16 of the patients the Schick test was carried out before immunization and their blood antitoxin titrated before and after treatment, with satisfactory immunization response in a majority, as shown in a table. No relation could be found between the antitoxin titre after the toxoid treatment and the clinical changes in the treated patients. In one group diphtheria toxoid alone was used and in three other groups this was supplemented respectively by an emulsion of the whole diphtheria bacillus, tubercle bacillus endotoxoid or a killed emulsion of a culture of a tubercle bacillus which had lost its acid-fast properties.

Tables are given of the results in all four series of cases. In Group I of 48 cases treated with diphtheria toxoid alone, four only showed marked improvement; all were neural cases which would have responded equally well to intradermal hydnocarpus ethyl esters. In Group II of 11 cases treated with toxoid and *C. diphtheriae* emulsion, the disease was not favourably influenced. Nor were satisfactory results obtained in smaller series of the other two groups. The treatment was voluntary, and only 71 of the 100 were willing to complete the full course, although leprosy patients will persevere with any treatment when they can observe any improvement. No improvement occurred in either body weight or the sedimentation test. Only five cases became negative bacteriologically, but six previously negative cases became positive while under the treatment. The results are summarized in the statement that out of 72 [? 71] who completed the course of diphtheria toxoid treatment, 12 became worse, 34 showed no appreciable clinical change, 21 showed slight improvement and 5 only a marked improvement, or 6·94 per cent. compared with 50 per cent. or more claimed by Collier in Thailand.

The authors remark that Collier's theory that suprarenal inefficiency was a necessary predisposing cause of leprosy seemed strange to them in view of the fact that not one case of such gross deficiency could be traced among nearly 5,000 leprosy cases that had passed through their hands. They therefore recorded the blood pressures in 100 unselected cases and found them to be entirely within the normal limits. Further, in eight successive post mortems in non-treated cases, no anatomical degeneration of the suprarenals could be discovered. They are unable to give any explanation for the very limited therapeutic results as compared with those claimed by Collier. *L. R.*

International Journal of Leprosy. Manila. 1941. Apr.–June. Vol. 9. No. 2. pp. 229–235. [17 refs.]—**Diphtheria Toxoid in Treatment and the Adrenal Injury Theory.**

Money (T. D. F.). **The Oji River Settlement and Clinics. Report on the Year 1940.**—*Leprosy Review.* 1941. Oct. Vol. 12. No. 4. pp. 79–89.

Cowdry (E. V.) & Ruangsiri (C.). **Influence of Promin, Starch and Heptaldehyde on Experimental Leprosy in Rats.**—*Arch. Pathology.* 1941. Oct. Vol. 32. No. 4. pp. 632–640. With 1 chart. [15 refs.]

The authors report on chemotherapeutic experiments in rat leprosy. Promin has been reported in the case of tuberculous guinea-pigs to lengthen life and reduce the lesions. Trials carried out in rat leprosy, with careful measurement of the lesions, showed that from about 60 to 140 days' treatment caused material diminution in the size of the leprous nodules, together with a united survival time increase of 1,258 to 1,583 days, but no material difference in the microscopical characters of the lesions. The injection of starch was followed by temporary healing in some nodules in controls as well. Injections of heptaldehyde into nodules had no beneficial effect. *L. R.*

TRYPANOSOMIASIS.

Reichenow (E.). Zur Frage der Bedeutung des Blepharoplasts der Trypanosomen. [**Function of the Blepharoplast of Trypanosomes.**] —*Arquivos do Inst. Biol.* Buenos Aires. 1940. Vol. 11. pp. 433–436.

The author discusses the function of the blepharoplast or kinetonucleus of trypanosomes and notes that as far as continued development in the vertebrate is concerned it appears superfluous, for *Trypanosoma equinum* and certain strains of *T. evansi* which are devoid of it can be passed indefinitely by blood inoculation from animal to animal. Whether this is true of development in the invertebrate has not yet been determined, though certain facts suggest that it may not be so. The trypanosomes which are most liable to lose the blepharoplast are those of the *T. evansi* group which are transmitted by flies mechanically. Those of *T. brucei*, *T. vivax* and *T. congolense*, which undergo cyclical development in their transmitting hosts, are much less liable to this modification. It is known, however, that if infected animals are treated with trypaflavin as many as 70 per cent. of the trypanosomes may lose the blepharoplast; and this loss having once been sustained, the blepharoplast does not reappear in subsequent passages. It would be of interest to test the possibilities of development of such a modified strain in tsetse flies but the experiment would be difficult to carry out. Some light might be thrown on the question by cultivation of a modified strain in the test tube. Accordingly the author subjected to the action of trypaflavin a strain of *T. gambiense* which he had shown to be readily cultured. When the trypanosomes in the animals had arrived at a condition in which 70 per cent. had no blepharoplast, culture was again attempted. This was just as successful as before but it was found that all the cultured forms possessed the blepharoplast. During two

months of culture no change was observed. As the culture appears to be an imitation of the development in the fly it would seem that the ablepharoplastic trypanosomes would be incapable of a cyclical development. *C. M. Wenyon.*

ROUBAUD (E.) & PROVOST (A.). Manifestations neurotropes d'une souche de *Trypanosoma gambiense* chez la souris. [**Neurotropic Manifestations of a Strain of** *Trypanosoma gambiense* **in the Mouse.**]—*Bull. Soc. Path. Exot.* 1941. Vol. 34. Nos. 1–3. pp. 48–50. With 1 fig.

Although as long ago as 1905 Plimmer observed in rats, infected with *Trypanosoma gambiense*, infections characterized by posterior paralysis and with trypanosomes detectable only in the spinal marrow, but little attention has been paid to the neurotropic manifestations of *T. gambiense* in the small rodent. It is generally considered that the infections in these animals are blood infections, varying according to the virulence of the strain employed.

In the present paper, the authors record some observations concerning a strain isolated from man in the Cameroons and since maintained in the laboratory by passage through guineapigs and mice. This strain has not become fixed for the animals in which it has been maintained. The infections are characterized by very great irregularity. In very young animals there is often an arrest of growth, but this phenomenon is not observed in animals some months old. In the latter, however, from time to time more or less pronounced posterior paralysis, with very few trypanosomes visible in the circulation, has been observed. Illustrations are given.

On the 18th August, 1939, two mice were inoculated subcutaneously with the trypanosome. In one, trypanosomes were seen in the blood fairly regularly. It died on January 4th, 1940, with numerous trypanosomes in the peripheral blood and without any paralytic signs. In the second mouse, very rare trypanosomes were seen in the blood on the 3rd, 5th and 11th September, but not again up to the time of death on the 15th May. In the middle of January this animal, however, presented paraplegic manifestations of the posterior limbs and intestinal incontinence. In the following month the posterior paralysis was complete. Although trypanosomes could not be seen in the peripheral blood after the 11th September, the blood inoculated into two mice, on the 4th and 28th February, 1940, infected a mouse on each occasion. A third attempt to infect mice, made on the 1st April, was negative. On the day of death, three mice were inoculated with an emulsion of brain, and one of them became infected.

The other observations recorded are comparable. The authors conclude that this particular strain of *T. gambiense* is clearly differentiated from other strains maintained for many years in the laboratory, by the irregularity of the infections and the neurotropic manifestations which it produced in mice. *W. Yorke.*

NASH (T. A. M.). **Bats as a Source of Food for** *Glossina morsitans* **and** *G. tachinoides*.—*Bull. Entom. Res.* 1941. Nov. Vol. 32. Pt. 3. p. 249.

Glossina morsitans and *G. tachinoides* are able to feed with ease on the bat *Nycteris hispida*, found in Nigeria. It is possible that when

floods force the game to evacuate the tsetse-infested river plain these bats form a very important source of food for the flies, especially *G. tachinoides*. *C. W.*

HAWKING (F.) & GREENFIELD (J. G.). **Two Autopsies on Rhodesiense Sleeping Sickness ; Visceral Lesions and Significance of Changes in Cerebrospinal Fluid.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1941. Nov. 29. Vol. 35. No. 3. pp. 155–164. With 5 figs. on 2 plates.

This paper describes post-mortem examinations made on two cases of *T. rhodesiense* sleeping sickness, the points of special interest being :—

" (1) No effective treatment to modify the natural development of the disease.

" (2) The marked visceral lesions.

" (3) The slightness of the lesions in the central nervous system and the correlation with the changes in the cerebrospinal fluid.

" (4) The concomitant infection with tuberculosis."

The first patient had been ill for six months. He complained of headache and pain in the chest. He was emaciated and could walk only with difficulty. The liver and spleen were moderately enlarged, as also were the lymphatic glands. The intelligence was fair ; there was no evidence of lesions of the central nervous system. Numerous trypanosomes were found in the blood. The cerebrospinal fluid contained trypanosomes, 14 cells per cmm., and 0·025 per cent. of protein. The patient was treated with undecane diamidine for 4 days, and the blood became free from trypanosomes but the cerebrospinal fluid remained unchanged. A few days later, trypanosomes reappeared in the blood ; the patient was given 1 gm. of germanin, but died 12 hours later. A detailed account of the post-mortem of this case is given, and the pathological changes are summarized as follows :

" Trypanosomal septicaemia.

" Inflammatory effusions containing trypanosomes in pleura, pericardium and peritoneum.

" Subacute inflammation of heart, principally myocardium and epicardium.

" Numerous trypanosomes in cerebrospinal fluid, but the tissues of the nervous system were practically normal and the meninges were only slightly involved.

" Tubercular consolidation of parts of both lungs, and tubercular foci in the mesenteric and other lymph nodes and in the liver and spleen."

The second patient had been ill for 4 months, with pains in the head, thorax, abdomen and legs. He was a very emaciated old man, who could stand and walk with difficulty only. The liver was enlarged, there was marked oedema of the ankles and the patient was demented. The blood contained numerous trypanosomes and the cerebrospinal fluid many trypanosomes, 10 cells per cmm., and the protein was 0·028 per cent. The patient was given 1 gm. of germanin, but died three days later. Here again, a full account of the post-mortem is given. The pathological changes are summarized as follows :—

" Trypanosomal septicaemia.

" Inflammatory effusions, containing trypanosomes in pleurae, pericardium and peritoneum.

" Subacute inflammation of heart, principally myocardium and epicardium. Numerous trypanosomes in C.S.F. ; but tissues and membranes of brain only slightly involved.

" Tubercular foci in lungs, liver, spleen and lymph nodes."

After discussing their findings, the authors give the following summary :

" Two autopsies are described of cases of *rhodesiense* sleeping-sickness, in which no appreciable treatment had been received. There were extensive trypanosomal effusions in the pleural, peritoneal and pericardial cavities, and marked inflammation of the myocardium, epicardium and endocardium. These visceral lesions were closely similar to those described by PERUZZI in the trypanosomiasis of monkeys. The cerebrospinal fluids of these cases contained numerous trypanosomes but the cell-count and protein content were not much raised ; corresponding to this pathological pattern in the fluid, the histological lesions in the central nervous system were very slight, being limited to a histiocytic infiltration of the cerebral membranes. From these cases and from experiments *in vitro*, it is concluded that it is not possible to have a true invasion of the cerebrospinal fluid by trypanosomes until the protein content is considerably increased. In the absence of treatment, the visceral lesions of *rhodesiense* sleeping-sickness are probably more often fatal than the lesions of the nervous system.

" These two cases also suffered from widespread infection with tuberculosis."

W. Y.

VAN ZYL (W. J.) & GEAR (James). **An Untreated Case of Trypanosomiasis.**—*South African Med. Jl.* 1941. July 26. Vol. 15. No. 14. pp. 278–280.

This paper gives an interesting account of the course of sleeping sickness in two brothers, who contracted the disease about the same time in 1939 near Maun, in Ngamiland, Northern Bechuanaland. One of the brothers was a faith healer by profession, and resolutely refused all treatment until he died, thus giving a unique opportunity to follow the natural course of the disease through all its phases, uninfluenced by drugs.

The two brothers entered the fly belt on the 9th July, and remained within it for six days. On the 12th and 13th July they were frequently bitten by tsetse, and they noticed that the bite marks differed from those received in other areas, in that they became swollen, hard and indurated, with purplish discoloration of the surrounding tissue. Both brothers apparently became ill about the 22nd July. The faith healer experienced cold shivers and developed a high fever, and later in the night became delirious. An erythematous rash was seen over his chest and back. His temperature remained high for five days, during which he was delirious. The acute symptoms then subsided, leaving him pale and weak, though shortly afterwards he was able to get up. On the 18th August, the possibility that he was suffering from trypanosomiasis was brought to the notice of the Public Health Department of Springs, and a visit was paid to his home. The patient, although up and about, appeared ill, and was pale and slightly emaciated. He complained of feeling weak. His skin was dry and his complexion sallow ; no rash was visible. The pulse was rapid and rather weak, the posterior cervical glands were enlarged but not tender, and the spleen was palpable but not tender. There was no marked abnormality in the nervous system, although a slight tremor was observed in the tongue and hands. On August 24th, numerous trypanosomes were found in the blood. In spite of every warning that the disease would end fatally and in spite of every persuasion, the patient persisted in his refusal to submit to treatment. For a month

and a half he improved considerably and was able to resume work, but two months after he had been first examined he complained of great weakness and recurrent digestive disturbances. Trypanosomes were again found in the blood. Thereafter the patient gradually got weaker and more debilitated. Signs and symptoms of nervous involvement appeared, and the patient was soon compelled to take to his bed. He had a convulsive attack on the 18th December, and died from congestion of the lungs and cardiac failure on the 23rd December, within six months of contracting the disease.

In contrast, the other brother, who apparently had no objection to drugs, was given seven injections of Bayer 205. He was discharged from the nursing home feeling perfectly well, and since that time, now 18 months ago, there has been no recurrence of symptoms. *W. Y.*

Brazzaville [Afrique Française Libre]: Rapport sur le Fonctionnement Technique de l'Institut Pasteur en 1940 [Ceccaldi (Jean), Director]. pp. 67–81—Service de la surveillance de la maladie du sommeil. [**Sleeping Sickness Service.**]

During the year 1940, one new case of sleeping sickness was found amongst 198 Europeans examined, and seven old cases have been kept under observation. The number of new cases found amongst natives was 209 ; of the 545 old cases kept under observation, 56 were discovered more than 10 years ago, 97 more than five years ago, and 380 less than five years ago. In the case of 12 others coming from the interior of the colony, it has not been possible to ascertain the date of their diagnosis.

Dealing with the disease amongst Europeans, it is recorded that the seven old patients have remained in excellent health. Clinical details are given of the new case discovered in 1940 and of a case discovered in 1939. These call for no comment.

Information is given regarding the method of diagnosis of the 209 new cases discovered amongst the natives, and of the methods and general results of treatment. In a table, the progress is shown of the 533 old cases, the date of infection of whom is known and who are still under observation. Of these, 140 appear to be cured, 258 are doing well, 103 are progressing, 9 have had blood relapses, 22 are dead, and one has been re-infected.

The paper ends with a description of the patient who was re-infected. This patient was found to be infected in 1929, when she was seven years old. She was treated with tryparsamide, and apparently cured. Numerous observations were made on her spinal fluid between March 1930 and January 1939. In June, 1940 she became ill, and lumbar puncture showed an excess of cells and of protein and the presence of trypanosomes. The author considers that the long period of observation, *viz.*, 10 years, in the course of which the patient appeared to be perfectly well and exhibited no signs of the disease, warrants the conclusion that it is a clear case of re-infection. *W. Y.*

van den Branden (M.). Considérations au sujet du séro-diagnostic de la trypanosomiase. [**Sero-Diagnosis in Trypanosomiasis.**]—*Bull. Soc. Path. Exot.* 1941. Vol. 34. Nos. 1–3. pp. 81–84.

Landsteiner and Scheer obtained complement-fixation reactions and positive flocculation reactions (Sachs-Georgi) in rabbits experi-

mentally infected with *Trypanosoma equiperdum* and also in rabbits injected with dead *T. equiperdum*. Somewhat similar observations have been made by other workers.

As the author had at his disposal rabbits infected for many months with *T. brucei*, he decided to examine whether he could obtain a complement-fixation reaction, either with antigen consisting of an alcoholic extract of *T. brucei*, or with the antigen of Bordet-Ruelens, which is an alcoholic cholesterin extract of the heart of a calf. In the preparation of the trypanosome antigen, the parasites were isolated by fractional centrifugation of the blood of infected rats and, after washing, were suspended in a mixture consisting of equal parts of pure glycerine and physiological saline. The fixation of the complement was established in doses of 0·2 cc. of serum inactivated at 56°C. for 45 minutes, and in doses of 0·05 and 0·025 cc. of antigen. In all the experiments the serum of normal rabbits was used as a control.

The maximum duration of the *T. brucei* infection in rabbits is 58 days, but the animals were kept alive beyond this limit by the administration of small doses of an antimonial. The infected animals were in good general health at the time the blood was removed. It appeared necessary to make the test on animals which had been infected at a certain time, in order that they might have had an opportunity of elaborating the immune bodies in their blood. The serum of guinea-pigs infected 12 days and of rats at the height of the infection always gave negative results. The serum of 11 out of 12 infected rabbits gave positive results. In the rabbit in which the reaction was anti-complementary, a positive reaction was obtained 15 days later, so that in reality all 12 animals gave a positive result. The serum of these rabbits did not give positive results with the artificial antigen of Bordet-Ruelens, and the normal rabbits likewise failed to give a positive result.

Four of the 12 infected animals were treated with Moranyl. Three weeks after the last dose the complement-fixation reaction was negative in all the animals. In order to see whether the reaction would occur with a non-specific antigen, van den Branden used an alcoholic extract of *T. equiperdum*. Of the eight rabbits infected with *T. brucei*, six gave a clearly positive reaction with the *T. equiperdum* antigen.

In conclusion, the author considers that these observations indicate the possibility of applying the complement-fixation reaction in the diagnosis of human trypanosomiasis, and for prognosis during treatment. The employment of a specific antigen for sero-diagnosis of human trypanosomiasis raises the difficulty, however, of obtaining a suitable antigen, because the blood of laboratory animals infected with *T. gambiense* is not sufficiently rich in parasites. *W. Y.*

HAWKING (F.) & SMILES (J.). **The Distribution of 4 : 4′-Diamidino Stilbene in Trypanosomes and Mice as shown by Fluorescence.**—*Ann. Trop. Med. & Parasit.* 1941. Oct. 21. Vol. 35. No. 1. pp. 45–52. With 5 figs. on 1 plate.

This paper describes the distribution of 4 : 4′-diamidino stilbene in trypanosomes and in the organs of mice, as shown by its fluorescence. When exposed to ultra-violet light, dilute solutions of the compound in distilled water show a brilliant blue fluorescence which is visible down to dilutions of 1/100 million to 1/1000 million. The technique used is described in detail, and the article is illustrated by a plate

showing the appearances, under ultra-violet illumination, of trypanosomes and of the organs of a mouse which have been exposed to diamidino stilbene.

The following summary is given :—

" 1. 4 : 4'-diamidino stilbene shows brilliant blue fluorescence when exposed to ultra-violet light. This property has been used to study its distribution in trypanosomes and in mice.

" 2. The compound is absorbed by (living) trypanosomes in large quantities ; it is deposited in the blepharoplast and in granules in the cytoplasm of the anterior portion of the organism.

" 3. In mice which have received the compound subcutaneously, it seems to collect especially in the liver and kidney and possibly also in the small intestine and skin. It is excreted in the urine, but probably not in the bile. Excretion in the urine is marked during the first seven hours after injection and ceases within two days.

" 4. Palmatine seems to collect especially in the pancreas, as shown by fluorescence under ultra-violet light."

W. Y.

MAYER (Martin). Ueber morphologische Veränderungen an Blutparasiten durch einwirkung Chemotherapeutischer Substanzen. Die Wirkung von Synthalin (Dekamethylen-Diaguanid) auf Trypanosomen und Leishmanien. [**The Morphological Changes in Blood Parasites caused by Chemotherapeutic Substances. The Action of Synthalin (Decamethylene Diguanidine) on Trypanosomes and Leishmania.**]—*Arquivos do Inst. Biol.* Buenos Aires. 1940. Vol. 11. pp. 229–234. [15 refs.]

The author reviews briefly previous work on the mode of action of drugs. He points out that as long ago as 1909 WERBITZKI, and shortly afterwards, others of EHRLICH's school showed that by the administration to infected animals of certain dyes belonging to the pyronin, acridin and oxazin series, and also of fuchsin and tryparosan, it was possible to produce blepharoplastless strains of trypanosomes. Subsequently, Mayer himself made a further contribution to the selective action of drugs on definite constituents of the parasite-cell when he showed that the first effect of germanin is to inhibit division of trypanosomes. The nucleus and the blepharoplast divide and sometimes also the flagellum, but the cytoplasm loses its capacity to divide, so that broad forms with two or several nuclei arise with remarkable prolongation of the posterior end and destruction of the flagellum apparatus ; finally, forms without blepharoplast or nucleus can be found.

This demonstration that different therapeutic substances acted on different parts of the cell gave rise to the idea that good results might be obtained by combined therapy of two differently acting substances. The work of STEFFAN (1922) showed that various dyes caused injury primarily to the cytoplasm of the parasite and that antimonials acted on the nucleus.

In malaria, the work of SIOLI and JAMES showed that the so-called atebrin-forms exhibited quite different appearances from the quinine-forms. According to James, the atebrin-forms show an aggregation of the pigment followed by its complete extrusion from the parasite, and the cytoplasm becomes thin, torn and vacuolated.

JANCSÓ, who showed that synthalin exerted a trypanocidal action, described the morphological changes produced by the compound ;

these closely resembled those produced by germanin. Mayer examined the action of synthalin in mice infected with *T. brucei* and *T. equiperdum*. He noticed that in blood films of the treated animals many blepharoplastless trypanosomes appeared, but he did not succeed in producing a permanent blepharoplastless strain similar to that resulting from the administration of the dyes mentioned above. Mayer believes that the action of synthalin is primarily on the blepharoplast, and thus differs from that of germanin.

The paper closes with a brief account of two experiments on the treatment by synthalin of hamsters infected with leishmania. In smears from liver puncture, many blepharoplastless parasites were seen. *W. Y.*

HUMPHREYS (Eleanor M.) & DONALDSON (Lilian). **Degeneration of the Adrenal Cortex Produced by Germanin.**—*Amer. Jl. Path.* 1941. Sept. Vol. 17. No. 5. pp. 767–775. With 4 figs. on 2 plates.

The possibility that germanin might injure the adrenal glands was suggested by the findings at autopsy of a patient with pemphigus who had been treated with this drug. In the present work, the authors have examined the point in experimental animals.

Germanin was administered to 100 guineapigs, 30 rats, 8 rabbits and 3 dogs, in the form of a 10 per cent. solution in freshly boiled distilled water. The drug used was the German product. The rats and most of the guineapigs were injected subcutaneously; in the other animals the drug was given by the intravenous route. All the animals were given adequate diets, and there was no evidence of vitamin deficiency in the control animals. The main part of this report summarizes the observations on 90 guineapigs, most of them young males weighing between 250 and 350 gm.

As the maximum single dose considered safe for the human adult is 1·0 gm. or 0·02 gm. per kilo., this dose, *viz.*, 0·02 gm. per kilo., was employed in the present experiments as the minimum single dose in serial injections imitating courses used in human therapy, while larger single and serial doses were used to ascertain injurious effects. Details of the dosages employed in the 90 guineapigs are given in a table.

The animals that died, and surviving animals, killed from 1 to 21 days after the last injection, were autopsied as soon as possible. Those showing pneumonia or other disease were excluded. The kidneys and adrenals were fixed and embedded together in order to standardize the planes of section and to permit rough comparisons of size. Usually sections of the liver and heart, and sometimes of other tissues, were prepared. Sections of kidneys, liver and heart were examined for fat.

Adrenal cortical lesions were found in 11 of 12 guineapigs which had received single injections of 0·1 to 0·4 gm. of germanin per kilo. These were constantly located in the outer part of the fasciculate zone, sometimes encroaching on the glomerular zone. The type characterized as an acute degenerative band was seen in four animals, all dying early after doses of 0·3 and 0·4 gm. per kilo., the established lethal dose for the guineapig. Lesions characterized as reactive bands

were seen in animals which survived doses of 0·1 to 0·3 gm. per kilo. It is interesting to note that no changes were found in the adrenals of guineapig no. 12, which was killed 21 days after an injection of 0·1 gm., a dose which invariably produced zonal lesions, and consequently it seems likely that the interval of three weeks had sufficed for complete healing.

Twenty guineapigs were given series of injections of single doses of 0·03, 0·05 or 0·1 gm. per kilo. each. Twelve of these were treated intensively with injections on alternate days, while in 8 the injections were spaced 8 days apart. Eleven animals of the former group died or were killed because they were moribund, while only two of the latter group died. The difference is especially significant because most of the members of the latter group were given larger single and total doses. The character of the zonal adrenal lesions, present in all, varied considerably. In some there were acute degenerative bands, in others there were mixed degenerative-reactive bands, whilst in still others, belonging to the group in which the doses were given eight days apart, there was a collapsed band appearance. These bands were narrow, devoid of epithelium and made up of stromal elements with wide capillaries lined by numerous flat endothelial cells. Here and there were a few lymphocytes and macrophages. There was no fibrous hyperplasia and the whole appearance suggested the condensation of a previously wider zone in which repair had been arrested. There was, however, some reparative activity at the borders, except in the animals which died.

The following are the conclusions :—

" Germanin in toxic doses consistently produces zonal degeneration of the adrenal cortex of small laboratory animals.

" Small serial doses of germanin, comparable to those in therapeutic use in man, may produce similar but less intense adrenal cortical lesions.

" It is probable that germanin has occasionally caused cytotoxic atrophy of the adrenal glands in patients with pemphigus.

" It is possible that other therapeutic agents may have a similar selective action and a capacity to injure the adrenal cortex."

W. Y.

KAMPMEIER (R. H.). **Urticaria due to Tryparsamide.**—*Arch. Dermat. & Syph.* 1941. Oct. Vol. 44. No. 4. pp. 671–673. [17 refs.]

" A case of generalized urticaria following the use of tryparsamide is reported. This reaction occurred on four separate attempts to use this form of therapy."

NASH (T. A. M.). **The Anchau Settlement Scheme.**—Reprinted from *Farm & Forest.* 1941. Oct. Vol. 2. No. 2. pp. 76–82.

This is an account of the origin and development of this rural settlement, situated in a sleeping sickness area. The many details concerning the problems dealt with cannot be abstracted, but the paper should be in the hands of all medical men and others interested in this aspect of the prevention of sleeping sickness. *C. W.*

MALBRANT (R.). Gibier, tsé-tsés et trypanosomiases. [**Game, Tsetse Flies and Trypanosomiasis.**]—*Bull. Serv. Zootech. Epizoot. A.O.F.* Dakar. 1940. Vol. 3. No. 3. pp. 187–202. [Summarized in *Rev. Applied Entom.* Ser. B. 1941. Oct. Vol. 29. Pt. 10. pp. 161–162.]

"The destruction of game as a method of controlling trypanosomiasis in Africa is discussed, and it is concluded that far from exterminating tsetse flies, which would be maintained on birds, reptiles, rodents and other animals not classed as game, such a course would force the flies to rely much more on man and domestic animals for food. Strong, Bequaert & Cleveland divide tsetse flies into three groups, typified by *Glossina palpalis*, R.-D., *G. tachinoides*, Westw., and *G. morsitans*, Westw., according to their relation with game, and a table is drawn up from data obtained by them showing the results of various workers who demonstrated that mammalian blood usually composed less than 50, about 70 and over 90 per cent. of the blood in flies of these three species, respectively. It is emphasised that the distribution of game and tsetses does not invariably correspond; the correspondence in the case of the *morsitans* group may be due not solely to a preference of the flies for game, but also to the fact that they are favoured by the same conditions as the latter. This is proved by the fact that when certain species of game begin their annual migration, the flies, even *G. morsitans*, only accompany them a short distance. Although the severe epizootics of rinderpest in South Africa that often exterminated herds of buffalo and antelope often coincided with the disappearance of *G. morsitans*, many non-susceptible animals survived and the tsetses could not have died of hunger. Evidence that some other factor intervened is provided by the fact that the tsetse disappeared at the same time from regions where the game had not been seriously affected.

"It is also suggested that the extermination of game would result in the adaptation to man of certain trypanosomes that at present are pathogenic to domestic animals only. The author considers that there is no proof that big game can be a reservoir of *Trypanosoma gambiense*; and that a study of the evolution of the foci of sleeping sickness caused by *T. rhodesiense* and the ease with which they can be stamped out in certain regions by the proper treatment of infected persons, without any change being made in the animal population, shows that game plays no part, or only an occasional one, in the conservation and propagation of this trypanosome. Various species of game can be reservoirs of trypanosomes pathogenic to domestic animals, and a table incorporating the results of many workers is given to show that the proportion of game animals harbouring trypanosomes in a region infested with tsetse flies is often considerable. It is thought, nevertheless, that the destruction of big game to remove one of the principal reservoirs of animal trypanosomiasis would not have the desired effect, as domestic stock also plays an important part and often harbours latent infection."

HORNBY (H. E.). **Immunization against Bovine Trypanosomiasis.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1941. Nov. 29. Vol. 35. No. 3. pp. 165–176. With 2 figs. [13 refs.]

This paper supplies information regarding the later fate of the animals which SCHILLING had attempted to immunize against trypanosomiasis. Schilling's general contentions were: "(1) That young

animals (foals, calves) in the first weeks of their life possess a considerable resistance against the African trypanosomes transmissible by tsetse flies ; (2) That this natural resistance can be enhanced to a full immunity against superinfections by the fly either by minimal infections or by preventive vaccine treatment." [This *Bulletin*, 1936, Vol. 33, p. 664.]

Schilling's conclusions are based on evidence of survival at the end of July, 1936, of three of 12 control animals, four of nine vaccinated cases, and eight of 17 calves treated with minimal infective doses. Schilling believed that the survivors were immune in the same way that most large African game animals within tsetse-fly belts are immune, that they could thus be maintained in the presence of tsetse, and that their offspring would be very good subjects for immunization.

In view of these widely-published high hopes, the subsequent history of the little herd is of interest. At the end of 1936, the experimental calves had become two-year-old heifers and bulls. They numbered 16 and, according to Hornby's notes, three of them were controls, four had been vaccinated with dead *T. brucei* and *T. congolense*, and nine had received minimal infective doses of *T. brucei*, *T. congolense* and *T. vivax*. In the same herd there were five cows—the remnant of the mothers of the experimental animals—and three calves born recently. The herd was maintained at Masumbwe, a village north of Tabora, in what was formerly a sleeping-sickness area of the Western Province of Tanganyika. Hornby inspected them on the 3rd December, 1936, and his findings are given in a table. At this time Masumbwe was at its best. There was abundance of grazing, and there were few, if any, tsetse about. The general appearance of the animals was excellent. Hornby was, however, not satisfied that the animals had been exposed to continual infection. He therefore planned to move the herd to an area where he knew they would be exposed to such infection, but before this was done, misfortune fell upon the herd.

On June 10th, 1937, Hornby received a telegram informing him that seven cattle had died and many others were sick. Blood smears from four of those which had died showed *T. congolense* and this parasite was also found in blood films from three of the remaining 17 animals. Shortly afterwards, Molloy reported on the survivors. He said that eight were definitely off-colour and presented the characteristic appearance of fly-struck animals. He failed to find any tsetse. By September 1937, the herd had picked up again, and Molloy found that only one animal was off-colour, all the rest being in good condition. Still no tsetse were seen. Smears taken every month showed that most of the animals were in a state of premunition regarding one or more species of trypanosomes, as usually two or three smears from animals which differed from month to month were positive for trypanosomes.

In July 1938, the herd was moved into unmistakable tsetse country, and from this time onwards the animals appeared to go downhill, many of them dying of trypanosomiasis. The last occasion on which Hornby saw the herd was the 21st January, 1941. Only six animals were still alive, and all were in poor condition—" a typically badly fly-struck little herd." Of the animals vaccinated or otherwise treated by Schilling in 1934, only one was alive. There was also one control. The other four were later calves of some of the mothers of the originally treated cattle. As they were born in light fly country, they were all infected naturally before they were a year old, and subsequently they

were exposed to repeated superinfections. During their short lives there had been times when, in spite of trypanosomes, they had regained a measure of good health. Yet they could not retain this state of premunition. Hornby concludes that there is nothing about the whole experiment to furnish hope that we are in sight of any practical method of immunizing cattle against trypanosomiasis. *W. Y.*

Wood (Sherwin F.). **New Localities for *Trypanosoma cruzi* Chagas in Southwestern United States.**—*Amer. Jl. Hyg.* 1941. July. Vol. 34. No. 1. Sect. C. pp. 1–13. With 7 figs. [18 refs.]

The object of this investigation was to collect and examine cone-nose bugs and bats from Texas for the presence of *Trypanosoma cruzi*. During the summer of 1939, 609 live Triatoma were obtained and 565 examined ; 30 (5·3 per cent.) were found to be naturally infected with *T. cruzi*. These included two *Triatoma protracta*, 20 *T. protracta woodi*, two nymphs of *T. gerstaeckeri*, and 6 *T. longipes*.

The author summarizes his observations as follows :—

" 1. Five new localities for the discovery of naturally infected *Triatoma* with *Trypanosoma cruzi* were found.

" 2. Three localities for *Trypanosoma vespertilionis* in bats were discovered.

" 3. Naturally infected *Triatoma longipes* and *T. protracta woodi* are reported for the first time.

" 4. Experimental infection of *Triatoma heidemanni* and *T. indictiva* is reported.

" 5. Preliminary testing in *Mus musculus* and *Peromyscus californicus insignis* of three new strains of *T. cruzi* showed evidences of greatest virulence for the Arizona (Congress) strain.

" 6. Developmental stages of *Trypanosoma cruzi* were demonstrated for the first time in the Eaton Canyon (Calif.) strain.

" 7. The first death of a white mouse due to infection with a strain (Eaton Canyon, Calif.) from the United States was reported.

" 8. Intimate human relationships with infected *Triatoma* were found.

" 9. Unilateral palpebral edema in man in infected areas of the United States should be viewed with suspicion as probable evidence of Chagas' disease."

W. Y.

Toranzos (Lazaro B.), Figuerero (Manuel L.) & Barbara (Luis). Primer caso agudo de enfermedad de Chagas en el departamento de Mercedes, provincia de Corrientes. [**First Record of Acute Chagas's Disease in Mercedes, Prov. Corrientes.**]—*Semana Méd.* 1941. July 17. Vol. 48. No. 29. pp. 149–151. With 1 map, 1 fig. & 1 chart.

The case occurred in a child of $5\frac{7}{12}$ years and presented the usual features. The parents were asked to forward for examination bugs from the house. Two females, a nymph and a larva were sent on one occasion, and a little more than a month later, a male and three females ; all these proved to be uninfected. More were asked for 3 weeks later and a female, five males and a nymph were sent and three of these were passing in the dejecta metacyclic and crithidial forms of the trypanosome. *H. H. S.*

TORREALBA (J. F.). Resumen de la práctica del xenodiagnóstico para la enfermedad de Chagâs en Zaraza (Guárico, Venezuela). [**A Review of Xenodiagnostic Work with Chagas' Disease in Zaraza, Venezuela.**]—*Rev. Med. Vet. Parasit.* Caracas. 1940. Vol. 2. No. 1–2. pp. 25–43. With 4 plates. [38 refs.] [Summarized in *Rev. Applied Entom.* Ser. B. 1941. Nov. Vol. 29. Pt. 11. p. 172.]

" Having observed that rural dwellings in the district of Zaraza, in the State of Guárico, Venezuela, were infested with Triatomids infected with *Trypanosoma* (*Schizotrypanum*) *cruzi*, the author has, since 1933, made 66 examinations for Chagas' disease by the method of xenodiagnosis, obtaining 22 positive results. The bugs used were *Rhodnius prolixus*, Stål, and in a few cases, *Triatoma* (*Eutriatoma*) *maculata*, Erichs. Records of the cases are given."

PIFANO (Félix). La enfermedad de Chagas en el Estado Yaracuy, Venezuela. [**Chagas's Disease in the State of Yaracuy, Venezuela.**] —*Gac. Med. de Caracas.* 1941. Feb. 15 & 28, Mar. 15 & 31 & Apr. 15. Vol. 48. Nos. 3, 4, 5, 6 & 7. pp. 201–206; 209–216; 220–227; 232–236; 244–246. [70 refs.]

The writer of this thesis was awarded the Vargas Prize for the period 1938–40. He has presented a fairly comprehensive account of the disease in Yaracuy. The subject is dealt with under 7 headings and ends with a list of 70 references. The author begins by giving a few clinical notes on 19 cases diagnosed by direct blood examination, and on 40 whose blood was negative and on whom the xenodiagnostic test was made; 14 of them proved positive. Next, he made a collection of the Triatomidae of the district and found 7 species, namely *Rhodnius prolixus, Eutriatoma maculata, E. nigromaculata, Psammolestes arthuri, Panstrongylus geniculatus, P. rufotuberculatus, Eratyrus cuspidatus.* Of these the most important (as the source of the most virulent strain of the trypanosome or being the most heavily infected) was *Panstrongylus geniculatus.* A third section concerns the animals found naturally infected—armadillo, opossum, cat, dog, rat and others. Only a few of these were examined, but all of 10 species were found infected. [In a table is given the percentage of each species infected, " 50 per cent " of 2, " 33·33 per cent. " of 3, each meaning, of course, one animal infected. This is very liable to mislead. In only two were more than ten examined, *viz.*, 16 *Canis familiaris*, of which five were infected—stated as 31·25 per cent.—and 19 *Hemiderma perspicillatum* of which 38 per cent. were positive—an impossible percentage, but probably means 7 of the total.]

In section IV the author discusses very briefly the relations between human and animal infection on the one side and naturally infected Triatomidae on the other. Next follow a few paragraphs on cultivation of the trypanosome and on the strains isolated, and less than 30 lines on treatment. Bayer 7602, recommended by Professor Salvador MAZZA, was given and " some of the clinical signs seemed to recede after the fifth dose (fever, adenopathy, splenomegaly and oedema)." The heartening effect of this statement is somewhat marred by the following, " But we observed like results in other patients studied by us who did not receive any treatment."

After a short epitome of the previous sections the author ends with a bibliography with references from Carlos Chagas's original work in 1909 to some of his own in 1940. *H. H. S.*

Gasic (Gabriel) & Bertín (Victor). Epidemiologia de la enfermedad de Chagas en Chile. [**Epidemiology of Chagas's Disease in Chile.**] —*Rev. Chilena de Hig. y Med. Preventiva.* 1940. June. Vol. 3. No. 1. pp. 5–30. With 2 plates. [171 refs.]

The first part of this article treats of Chagas's disease on general lines—the trypanosome, its vector, animal reservoir hosts, wild and domesticated. The latter part deals with the distribution of the disease in Chile, the ages of those attacked (half were between 6 and 10 years), the seasonal prevalence (more than half in the first half of the year), and serological diagnosis.

The transmitting Triatomidae are widespread in the northern and central parts of Chile; how far they extend to the south has not yet been determined. Of more than 7,000 specimens of *Triatoma infestans* examined, round about 40 per cent., mainly in the provinces of Atacama, Coquimbo, Santiago and Aconcagua, have been found infected. Dogs and cats have been found naturally infected. The Machado Guerreiro reaction has proved very reliable; among 416 persons in the small district of Domeyko, 32·4 per cent. gave clear positive reactions. *H. H. S.*

Neghme (Amador) & Faiguenbaum (Jacobo). Observaciones preliminares sobre enfermedad de Chagas, en la parte alta del valle del Rio Aconcagua. [**Chagas's Disease in the Upper Parts of the Aconcagua Valley.**]—*Rev. Chilena de Hig. y Med. Preventiva.* 1940. June. Vol. 3. No. 1. pp. 57–59.

This is little more than a preliminary note. On the right bank of the valley runs the Chile-Argentine railway and there are many scattered dwellings, inhabited mostly by railway employees, along the route. The authors have examined so far 303 Triatoma specimens in various stages of development and found 89, or 29·3 per cent., infected by *T. cruzi*; 55 were in the imago stage, 33 nymphs and 1 larva. Children are seen showing Romaña's sign—unilateral palpebral oedema. Further study is to be undertaken. *H. H. S.*

Sinjovich (Isaac) & Somaini (Antonio F.). Un caso de enfermedad de Chagas en Clodomira. (Pcia. de Santiago del Estero.) [**A Case of Chagas's Disease in Clodomira, Santiago del Estero.**]—*El Dia Médico.* Buenos Aires. 1941. July 7. Vol. 13. No. 27. pp. 626–627. With 3 figs.

A typical case in a boy, 4¼ years old, proved by finding of the trypanosome in a thick drop preparation, and cured by paroxyl (0·02 gm. per kilo. body weight) and dicalose and arrenal 0·1 gm. daily. At the end of a week after he came under the authors' observation, the oedema of the eye had disappeared, neither liver nor spleen was palpable and the general state was good. The child was discharged from hospital 11 days after admission and "subsequent examinations at the laboratory have revealed no abnormality." *H. H. S.*

Rey-Matiz (Hernando). Observaciones sobre trypanosomas en Colombia. [**Trypanosomes of Colombia.**]—*Rev. Facultad de Med.* Bogota. 1941. July. Vol. 10. No. 1. pp. 25–49. With 20 figs. [25 refs.]

Rosenfeld (Gastão) & Cardoso (Francisco A.). Distribuição dos triatomideos e da moléstia de Chagas no estado de São Paulo (Brasil). [**Triatomidae and Chagas's Disease in São Paulo.**]—Reprinted from *Rev. Clin. de S. Paulo.* 1941. Vol. 9. No. 6. pp. 198–209. With 2 maps. [31 refs.] English summary.

After a brief review of the literature regarding the presence of Chagas's disease in S. Paulo, the authors give a list of the vectors found infected in nature, together with a map of the State showing by difference of shading the municipalities or counties: (1) where no Triatomidae were seen, (2) where they were found but not infected, and (3) where infected bugs were present. The species identified were: *T. infestans, T. rubrofasciata, Eutriatoma oswaldoi, E. sordida, E. tibiamaculata, Panstrongylus megistus, P. geniculatus* and *Rhodnius domesticus*. The first was the commonest.

On a second line-map are indicated the municipalities with the distribution of Triatomidae, of human cases of the disease and of the animals found infected in nature. Two hundred and seventy municipalities were investigated, and in 92 of them Triatomidae were found; in 41 these insects were proved to be infected by *T. cruzi*. Distributed among seven municipalities 11 human cases were found, and in two there were found three domestic dogs infected. *H. H. S.*

Mazzotti (L.). **Experimental Infection of** *Haematosiphon inodora* **Dugès with** *Trypanosoma cruzi* **Chagas.**—*Bull. Brooklyn Ent. Soc.* Lancaster, Pa. 1941. Vol. 36. No. 2. pp. 67–68. [Summarized in *Rev. Applied Entom.* Ser. B. 1941. Dec. Vol. 29. Pt. 12. p. 191.]

" On 20th June 1940, 15 adults of *Haematosiphon inodorus*, Dugès, a Cimicid that infests poultry yards in Mexico and the United States and attacks man as well as fowls, especially when the yards are near bed-rooms, were placed on a mouse lightly infected with *Trypanosoma cruzi*; 12 of them fed in about 20 minutes, and 4 defaecated less than 5 minutes after feeding. One of the bugs was killed on 5th July and metacyclic forms of *T. cruzi* were numerous in its intestinal contents. Saline suspensions of the intestinal contents of two of the infected bugs were inoculated intraperitoneally into two mice on 11th July, and both the mice became infected, the incubation periods being 11 and 15 days."

Pifano (Felix). Parasitismo natural de Amblyomma Longyrostre Koch, 1844 por *Schizotrypanum cruzi* Chagas, 1909. [*Amblyomma longyrostrum* **Infected in Nature by** *T. cruzi*.]—*Gac. Méd. de Caracas.* 1941. May 31. Vol. 48. No. 10. pp. 288–289.

The author in the course of an examination of the ectoparasites of Cercolabidae in the State of Yaracuy, Venezuela, found *Amblyomma longirostrum*, a parasite of the porcupine, naturally infected with *T. cruzi*. In the larval and nymph stages it is commonly found in birds, but the adults are more usually seen on tree-dwelling animals and especially the Cercolabidae (arboreal porcupine). *H. H. S.*

Cardosa (F. A.) & Navajas (E.). Achado de dois cães naturalemente infectados pelo *Trypanosoma cruzi* Chagas, 1909, no município de Itaporanga, Estado de São Paulo. Presença na mesma localidade de *Triatoma infestans* (Klug, 1834), infectado pelo *T. cruzi*. [**Two Dogs Infected with** *T. cruzi*; **Infected** *T. infestans* **in the State of São Paulo.**]—Reprinted from *Rev. Clin. de S. Paulo*. 1941. Vol. 9. No. 6. pp. 179–187. With 14 figs. [11 refs.] English summary.

"The authors give the results of a survey on Chagas' disease which was carried on in the Nucleo Colonial 'Barão de Antomina,' municipality of Itaporanga, State of S. Paulo, Brazil. They captured 540 triatomids belonging to *Triatoma infestans* (Klug, 1834), which were examined and found infected with *Trypanosoma cruzi* Chagas, 1909, in a high percentage (45·3 per cent.). They also found two dogs naturally infected by *T. cruzi*, and based diagnosis on thick blood drop examinations. Search for human cases was negative."

Torrealba (J. F.) & Riccardi (Blas). Más notas clínicas y epidemiológicas acerca de la enfermedad de Chagas. [**Chagas's Disease. Clinical and Epidemiological Notes.**]—*Gac. Med. de Caracas*. 1941. Mar. 31 & Apr. 15. Vol. 48. Nos. 6 & 7. pp. 238–241; 246–248. With 8 figs.

The authors record four cases briefly, a female child of 11 months, a girl of 16 years and two adult women. All four presented Romaña's sign with dacryo-adenitis and the trypanosome was found in a thick drop of blood in each case. The patients came from Palo Seco and Tablerito, suburbs of Zaraza. Eleven of the inhabitants were tested by xenodiagnosis and two proved positive. *Panstrongylus geniculatus* was found in the nests of the armadillos, and of two adults, three larvae and two nymphs of *P. geniculatus* all were infected with *T. cruzi*. Dogs (15), pigs (3) and cats (4) were examined by thick blood drop or the xenodiagnostic method, and one cat proved positive by the latter; all the rest were negative. Other reservoir hosts were found to be armadillos, grey rats and wild guineapigs (acure).

H. H. S.

Mazza (Salvador) & Salica (Pedro R.). Investigaciones sobre enfermedad de Chagas. Acerca de *Chagomas hematógenos*: en un caso simulando abscesos múltiples y en otro chagoma de inoculación. [**Studies in Chagas's Disease. Haematogenous Chagomata.**]—*Universidad Buenos Aires: Misión de Estudios de Patología Regional Argentina (Jujuy). Publicación No. 54.* 1941. 21 pp. With 18 figs.

The authors divide chagomata into three types: (1) Chagoma of inoculation, *i.e.* a swelling at the site of primary inoculation. (2) Metastatic chagomata, satellites of the primary chagoma. (3) Haematogenous chagomata, multiple and probably blood-borne, appearing at a distance from the primary chagoma. A subvariety of the last—a swelling with deep cellulitis appearing on the face—are designated *Lipochagomas genianos*, or lipochagoma of the cheek.

They describe two cases, in one of which, in a child of two months, several chagomata appeared on the trunk and were opened and discharged purulent matter (but the blood picture showed a lymphocytosis

of 50 to 64 per cent. and polymorphonuclears 38 to 18 per cent. only). The second patient was a girl of two years and four months with a swelling " the size of an orange " over the left side of the face and angle of the lower jaw.

The histology of the condition is well depicted in photomicrographs. Briefly, it is characterized by marked inflammation of the skin and cytosteatonecrosis of the subcutaneous tissues. In the histiocytes leishmanial forms of *T. cruzi* are demonstrable. *H. H. S.*

Mazza (Salvador), Basso (Germinal) & Basso (Redento). Investigaciones sobre enfermedad de Chagas. Comprobación por biopsia de la naturaleza chagásica de la esquizotripanide eritematosa polimorfa. [**Chagas's Disease. Histological Proof of the Trypanosomal Nature of the Erythematous Eruption in this Disease.**]—*Universidad Buenos Aires: Misión de Estudios de Patología Regional Argentina (Jujuy). Publicación No. 56.* 1941. 29 pp. With 27 figs.

A man of 36 years, living in Mendoza, developed Chagas's disease, with a primary chagoma of the neck and on the 10th day an erythematous eruption on trunk and limbs, the so-called roseola or polymorphic erythema of this disease. On the 17th day of disease, the eighth of the rash, a specimen of a prominent site of the rash was taken for biopsy examination and leishmanial forms of the trypanosome were demonstrated. Photographs are reproduced showing the rash and its distribution, the primary chagoma and the histology of the cutaneous lesions. *H. H. S.*

Caceres (Romeo). Acerca del " signo del ojo " o " signo de la M.E.P.R.A." en la enfermedad de Chagas. [**The Eye Sign or the M.E.P.R.A. Sign in Chagas's Disease.**]—*Prensa Méd. Argentina.* 1941. Sept. 10. Vol. 28. No. 37. 7 pp. With 1 fig.

This is usually known as Romaña's sign; the initials indicate the *Misión de Estudios de Patologia Regional, Argentina.* *C. W.*

Mazza (Salvador). Tratamiento de la enfermedad de Chagas. [**Treatment of Chagas's Disease.**]—*Prensa Méd. Argentina.* 1941. July 30. Vol. 28. No. 31. 7 pp.

Chagas (Carlos). Tripanosomiasis americana. Versión castellana, introducción y notas de: Memorias do Instituto Oswaldo Cruz, Tomo VIII, Fascículo II, año 1916, por Salvador Mazza. [**American Trypanosomiasis.**]—*Universidad Buenos Aires: Misión de Estudios de Patología Regional Argentina Jujuy. Publicación No. 55.* 1941. 45 pp. With 16 figs.

MALARIA.

ALEXANDROV (Y. M.). **Malaria in the Mountains.**—*Sovet Med.* 1940. No. 2. pp. 19-20.

This contribution is based on the experience of the author in the Pamirs in regions at an altitude of not less than 2,000 m. It has been observed that malarial subjects, be the infection active or latent, generally develop an acute paroxysm or exacerbation on journeying from low levels into the mountains. The quicker and greater the change of altitude the greater is the tendency to and severity of the attack. A journey by air at 4,000 m. is more likely to precipitate a paroxysm than a car journey. Though the disease is either activated or exacerbated, high altitudes have a favourable influence on the disease; often it is seen to terminate with the precipitated paroxysm or to undergo favourable changes in the symptoms; the enlarged spleen shrinks to its normal size.

The mode of action of the various factors concerned is not sufficiently studied and understood. Heightened ultra-violet radiation, oxygen hunger, rapidity and height of ascent, fatigue of the journey, all have a share in precipitating the paroxysm of malaria. Quartz radiation is known to provoke an attack and is used as a diagnostic test for latent disease. The author attributes the beneficial effect of altitude on the patient to the marked stimulation of vitamin D formation, activation of bone-marrow and haemopoiesis.

The precipitation of the attack is accounted for by the plasmodia thrown into the circulation from the blood squeezed out of the shrinking spleen. The lowered atmospheric pressure explains the epistaxis and copious menses seen in some patients. The water of mountain springs, being rich in salts, sometimes upsets the digestive tract and brings about a relapse of malaria.

The author has often encountered tertian malaria in the Pamirs even in winter. Anopheles are found at altitudes of 2,000 m.

The author's findings are based on some 200 cases among copper miners and alpinists in this region. Among diseases calling for differential diagnosis he includes typhoid, central pneumonia, miliary tuberculosis, meningitis, typhoidal influenza [*sic*], typhus, visceral leishmaniasis, syphilitic fever, sandfly fever and brucellosis. He draws special attention to relapsing fever due to *Spirochaeta carteri*, which is most confused with malaria in this region. The spirochaetal fever is self-limited, ends in immunity of the patient, and is said to have no specific remedy. In some cases both infections may be present. The author states that blood tests cannot be relied on for diagnosis, as they vary with the altitude, but considers that Henry's reaction is of reliable diagnostic value.

To combat malaria in the Pamirs, the author advocates compulsory prophylactic treatment with acri-quinine [atebrin] in all cases of less than three years' freedom from attacks. In active cases, owing to the probability of concurrent infection with both malaria and *Spirochaeta carteri*, simultaneous treatment with Orasol and plasmocide is recommended. Cardiazol and barbiturates have been valuable in ameliorating the patient's condition. *D. V. Giri.*

TANAKA (Shigeo). Untersuchungen der hygienischen Gegeustände in der Yulin-Gegend auf der Insel Hainan. [**Health Conditions in the Yulin District of Hainan.**]—*Taiwan Igakkai Zassi* (*Jl. Med. Assoc. Formosa*). 1941. July. Vol. 40. No. 7. [In Japanese pp. 1181–1208. With 4 figs. on 1 plate. [53 refs.] German summary pp. 1208–1211.]

Malaria is endemic in the Yulin district of Hainan, but the inhabitants are cut off from treatment, and preventive measures are unknown. It is an area of streams from the foothills, and through it flows the sluggish river Taginsui, whose banks are thickly wooded. The mean temperature is from 24·5°C. to 28·6°C. and the relative humidity over 50; there is a heavy rainy season. The Anopheles found were *A. hyrcanus* var. *sinensis* (132 specimens), *A. jeyporinensis* var. *candidiensis* (101), *A. maculatus* (23), and *A. annularis* (78). [No mention is made as to infection in these species, or as to their breeding places.] Malaria parasites were found in 6·1 per cent. of the persons examined, *P. vivax* and *P. falciparum* about equally. Enlarged spleens were found in 34·3 per cent. of the total examined, but in 64·2 to 75 per cent. of children under 15. In general there was slight anaemia with a colour index of 0·93.

The remainder of the paper deals with various blood examinations in which nothing new is recorded. *C. W.*

VISWANATHAN (D. K.). **The Utility of Malaria Parasite Indices in Infants in the Study of Malaria.**—*Jl. Malaria Inst. of India.* 1941. June. Vol. 4. No. 1. pp. 139–152. With 2 graphs. [10 refs.]

This is a study based on the results of the examination of the blood of 1,697 infants under one year of age living on tea estates in Upper Assam where *A. minimus* is the vector. Of this total 393 were found to be infected, 23·2 per cent., as compared with a parasite rate of 46 per cent. in children from 2 to 10 years of age. The infection rate for infants increased with age: 6·0 per cent. below two months; 14·9 from two to four months; 32·4 from four to six months; 47·9 per cent. six monthly or over. The age and seasonal distribution of the positive findings indicated that there is a prolonged period of transmission from May to January inclusive and that relapses are most prevalent in April; that *P. vivax* transmission commences in May and that *P. vivax* infections are most prevalent from May to July; that *P. falciparum* infections are more prevalent than *P. vivax* infections throughout the year and are most prevalent in the last quarter of the year; and that infants under two months of age seem to possess some degree of inherited immunity. The author considers that infants of the age-group more than two but less than four months furnish the best evidence of the quantum of seasonal infection.

Norman White.

RAMON (T. K.). *Plasmodium ovale* **in India.**—*Jl. Indian Med. Assoc.* 1940. Sept. Vol. 9. No. 12. pp. 583–585. With 6 figs.

The author writes to say that several protozoologists in India have seen slides from the patient, and have confirmed his opinion that the parasite was typical *P. ovale* [see this *Bulletin*, 1941, Vol. 38, p. 290].—*Ed.*

MARKS (M. B.). **Accidentally Transmitted Malaria.**—*Arch. Pediatrics.* 1941. June. Vol. 58. No. 6. pp. 357–364. [18 refs.]

A two-months-old infant developed an attack of quartan malaria in hospital at Miami, Florida, after receiving three intramuscular injections of whole blood. The donors of the blood were the father of the infant and a laboratory technician. Neither the father nor the technician had any history of malaria nor did an examination of their blood give any evidence of malaria infection. The mother also denied having suffered from malaria. The author considers it most improbable that the infant could have been infected in the usual way. Though the evidence is very inconclusive the author considers it probable that the blood transfusions were responsible for the infection. He considers it wise to exclude all donors who have ever had malaria or who come from malarial regions. If this be impossible he recommends that the recipient should be given a course of atebrin as a prophylactic measure. [For the use of quinine for this purpose, see this *Bulletin*, 1941, Vol. 38, p. 505.] *N. W.*

GORDON (Ernest F.). **Accidental Transmission of Malaria through Administration of Stored Blood.**—*Jl. Amer. Med. Assoc.* 1941. Mar. 22. Vol. 116. No. 12. pp. 1200–1202. With 1 chart.

There are some 35 instances on record in which malaria has been transmitted by the transfusion of fresh blood, but the case reported here is the first in which malaria has been found to have been accidentally transmitted by a transfusion of stored blood.

The patient, a boy aged seven, received three transfusions of stored blood for the relief of anaemia secondary to sepsis. Forty-four days after the first transfusion and 33 days after the last, he developed recurrent attacks of fever. After a further two to three months he was re-admitted to hospital. A tentative diagnosis of malaria was confirmed by the finding of numerous quartan malaria schizonts in a stained thick blood smear. The patient was treated with atebrin and made a good recovery.

Since the boy resided in a district where malaria is almost unknown, it seemed likely that one of the blood transfusions might have been responsible. Two donors were concerned; whereas one had lived in a district free from malaria, the other had lived in Italy for the first 15 years of his life and had also been in France during the first World War. The blood of both donors was examined after both had received an injection of adrenalin. A few malaria parasites were found in the blood of the Italian-born donor. The blood of this donor had been stored for only two days before being used for transfusion.

Previous experimental work suggests that malaria can be transmitted *via* stored blood when the blood has been stored for less than five to eight days. The author suggests that the accidental transmission of malaria by transfusion could be avoided either by only using blood stored for more than eight days, or by examining a thick smear of the blood of all prospective donors, or by refusing to accept as donors any individuals who have ever resided in a district where malaria is endemic.

[The possibility that the Italian-born donor might have been re-infected whilst resident in the U.S.A. is not discussed. Blood taken

from individuals who have previously lived in malarial districts may safely be used for the production of serum and plasma.]

P. L. Mollison.

Raevskii. **[The Microclimate of the Winter Quarters and the Behaviour of the Hibernating Females of *Anopheles maculipennis* var. *messeae*, Flni.]**—*Vopr. Phisiol. Ekol. malar. Komara.* Moscow. 1940. Vol. 1. pp. 135–151. With 3 figs. [Summarized in *Rev. Applied Entom.* Ser. B. 1941. Dec. Vol. 29. Pt. 12. p. 202.]

"From December 1934 to February 1935, the author studied the variations in the microclimate of an experimental winter shelter for *Anopheles maculipennis* var. *messeae*, Flni., and the behaviour of the females hibernating in it. The temperature in the shelter varied by 4–5°C. [7·2–9°F.] at various points; it was higher at the walls than the average for the shelter as a whole during the first half of the period and lower during the second. The overwintering females showed the same marked negative geotaxis as summer individuals. Relative humidity, which was above 60 per cent., did not influence the distribution of the mosquitos in the shelter. In the presence of fairly uniform temperature and humidity, light was the main factor, the mosquitos preferring the darkest places. In a relatively warm environment, they were in continuous slow movement. The behaviour of the overwintering mosquitos is classified as typical of summer, semi-hibernation and hibernation; the degree of complexity of the reaction to stimuli varied directly with environmental temperature. In relatively warm surroundings, the fat-body was rapidly exhausted, giving rise to weakness and consequent variation in the reaction to stimuli. Hibernation did not interrupt the tendency of some individuals to leave the shelter. As in summer, flight occurred at sunset and was probably due to hunger caused by premature exhaustion of the fat-body. The number of weakened individuals increased towards spring, and they came down from the ceiling and upper part of the walls and died."

Bates (Marston). **Field Studies of the Anopheline Mosquitoes of Albania.**—Reprinted from *Proc. Entom. Soc. Washington.* 1941. Mar. Vol. 43. No. 3. pp. 37–58. With 7 figs. (6 on 3 plates). [15 refs.]

Blacklock (D. B.) & Wilson (Carmichael). **Notes on *Anopheles gambiae* and *A. gambiae* var. *melas* in Freetown and its Vicinity.**—*Ann. Trop. Med. & Parasit.* 1941. Oct. 21. Vol. 35. No. 1. pp. 37–42.

This note is of some importance to Freetown. The authors confirm the suggestion made by Ross that engorged female anophelines may rest during the daytime in shrubs. Adult female *A. gambiae* were found in hedges (of a species of angelica) and young oil palms, and the finding of these led to the discovery of a breeding place in human footprints on a newly constructed slipway down to the beach. Seepage water had filled these small hollows, and they were crowded with larvae. Oiling of the breeding place and spraying of the hedges eliminated the mosquitoes.

A. gambiae var. *melas* was found also; of 30 dissected, two had microfilariae, one sporozoites in the glands and one both microfilariae and sporozoites.

C. W.

VENHUIS (W. G.). De vindplaatsen van geinfecteerde *Anopheles maculatus* tijdens een epidemie in Oost-Java. [**The Haunts of Infected** *A. maculatus* **during an Outbreak of Malaria.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1941. Oct. 14. Vol. 81. No. 41. pp. 2178–2188. With 2 figs. on 1 plate. [10 refs.] English summary.

During an epidemic of malaria at Kediri in East Java the author dissected 393 specimens of *A. maculatus* caught in houses, but found no stomach infections and only one sporozoite infection. This result was so poor that he conceived the idea that infected mosquitoes tended to leave the houses, and a second series of catches was made in the steep, shadowy and moist banks of the smaller streams. Here, of 124 guts examined, one was positive, and of 136 specimens 2 showed sporozoites. By this time the epidemic was almost at an end, and it is thought that if such a search had been made earlier, a larger number of infections would have been disclosed. Only about one-third of *A. maculatus* caught in houses contained blood, whereas practically all the females on the stream banks were engorged. It may be that the mosquitoes in the houses were largely young adults waiting for a blood meal, or that there are two biologically distinct varieties; no morphological differences were found in adults, larvae or pupae to support the latter theory. *C. W.*

WHITE (R. Senior). **Observations on the Adult Habits of** *Anopheles fluviatilis* **and** *Anopheles varuna.*—*Jl. Malaria Inst. of India.* 1941. June. Vol. 4. No. 1. pp. 57–62.

This work was carried out in the Satpura Mills, Central Provinces, and at Vizagapatam, Madras.

PATERNÒ (P.). Il midollo osseo nelle splenomegalie da malaria cronica o progressa. [**Bone Marrow in Malarial Splenomegaly.**]—*Minerva Medica.* 1940. Apr. 21. No. 16. pp. 346–351. With 1 fig.

FIELD (J. W.). **A New Rapid Method of staining Malarial Parasites in Thick Blood Films.**—*Bull. Inst. Med. Res. Federated Malay States.* 1941. No. 2. 16 pp. With 19 figs. on 4 plates. [15 refs.]

The author has already described in earlier publications [this *Bulletin*, 1940, Vol. 37, pp. 808 and 874] methods he has found useful as aids to the rapid staining and identification of malarial parasites in thick films. In this paper certain details and figures which did not appear before are given. It is perhaps noteworthy that the time of exposure of films to the stain has been lengthened to a slight extent but nevertheless, the whole of the staining process, illustrated by a series of drawings, occupies less than ten seconds. The drying of the thick film in the first place is given as five minutes and presumably a similar period is required for the stained film to dry as it stands in the vertical position before it is fit to examine. One section of the paper is devoted to the differential diagnosis of malarial parasites in thick films and three plates of micro-photographs illustrate the points emphasized. In an appendix an alternative method for preparation of the stain is described. *C. M. Wenyon.*

VAILLANT (C. M.). **Report on a Group of Cases of Benign Tertian Malaria which in the Early Stages simulated German Measles.**—*Jl. Roy. Army Med. Corps.* 1941. Nov. Vol. 77. No. 5. pp. 259–260. [Summary appears also in *Bulletin of Hygiene.*]

A convoy of 20 patients from the same unit in the Sudan arrived in hospital, each man with a rash and fever. The diagnosis of German measles was made both at the unit and the hospital, though no patient showed enlarged glands ; the rash was typical of that condition. The fever did not fall, however, and enlargement of the spleen was present in 6, so that blood examination was performed and in each case *P. vivax* was found. Later, more similar cases arrived, making a total of 50. The fever and the rash disappeared under treatment with quinine.

It is beyond the limits of probability that all cases of German measles should have had malaria and *vice versa*, but such a rash in malaria is almost unknown ; the opinion of two consultants was that these were cases of malaria with prickly heat brought on by the excessive sweating during the paroxysms, but in view of the fact that the diagnosis of German measles was made and malaria not at first suspected, these cases are important. [They also provide an argument in favour of the routine examination of the blood in all fevers in malarious areas.] *C. W.*

CHOPRA (R. N.), SEN (B.) & GUPTA (J. C.). **Induced Malaria with Heavy Malignant Tertian Infection.**—*Indian Med. Gaz.* 1941. June. Vol. 76. No. 6. pp. 350–352.

The patient, suffering from tabes dorsalis, was inoculated with blood containing scanty *P. vivax* and *P. falciparum*, but as no reaction occurred, he was given a second injection a month later. This produced an attack of subtertian malaria, which is described, and in which scanty rings only were seen for a week ; after that time the intensity suddenly developed to an infection of 30–40 per cent. of red cells. An intravenous injection of 7½ grains of quinine reduced this to 2 or 3 rings only per field and the infection was controlled in a few days by quinine given intramuscularly and by the mouth.

In India, where benign tertian infection is so common, Chopra has often used blood infected with *P. falciparum* in the treatment of neuro-syphilis, but points out that careful daily observation and blood examination are essential. It is also noted that *P. falciparum* infection induced by blood injection is much more easily controlled than is infection transmitted by mosquitoes, though not so easily as *P. vivax* inoculated in blood. A warning is given that in blood mixed infection is common and *P. falciparum* may suddenly flare up in the course of what appears to be a *P. vivax* infection. *C. W.*

KLIGLER (I. J.) & YOELI (M.). **The Diagnostic and Epidemiological Significance of the Complement Fixation Test in Human Malaria.**—*Amer. Jl. Trop. Med.* 1941. July. Vol. 21. No. 4. pp. 531–543. With 1 fig.

For their complement fixation tests the authors used as antigen dried monkey blood infected with *P. knowlesi* that was given them by COGGESHALL [see this *Bulletin*, 1939, Vol. 36, p. 926]. It was used in

a dilution of 1 : 160. An examination of sera from 309 human cases of malaria was made. As a rule the reaction became positive during the third week after the onset, if the patients had had two or more attacks. Patients cured after one attack failed to give a positive reaction. In a few cases observed continuously the reaction disappeared during the fourth month after the last attack. In a hyperendemic area 98 per cent. of the children up to 12 years of age gave positive reactions regardless of the presence of parasites in the blood at the time of the test. Infected adults in this area also gave positive results. Only 10 per cent. of healthy adults in this area gave positive reactions.

A few tests were also made with an antigen prepared from *P. gallinaceum*. There is a cross reaction between the antigens of *P. knowlesi* and *P. gallinaceum* and sera from human cases of malaria that gave positive reactions with *P. knowlesi* antigen did so also with *P. gallinaceum* antigen. *N. W.*

D'Alessandro (G.) & Sicari (S.). Sull'essenza della reazione di Henry. [**Intrinsic Nature of Henry's Reaction.**]—*Riv. di Malariologia.* Sez. I. 1941. Jan.–Feb. Vol. 20. No. 1. pp. 1–7. German summary.

The object of the research described in this paper was to determine whether Henry's reaction has any real immunological significance, or in other words whether the globulin of the serum of a malaria patient possesses any specific, or pseudospecific, affinity for melanin. The experiments recorded seem to supply an affirmative answer to this question ; the authors believe that the reaction is more than a pure and simple physico-chemical reaction.

Recourse was had to the complement fixation technique. Tests were made with several substances: Globulin precipitated from serum with distilled water ; euglobulin precipitated from serum with N/250 HCl ; the supernatant liquid of the euglobulin deposit neutralized with NaOH ; and whole serum, of both Henry positive and Henry negative sera. These were compared with regard to their power of deviating complement with a 1 : 20 dilution of melanin. The only difference noted between malaria and non-malaria sera was confined to the globulin fractions precipitated with distilled water : the globulin from malaria serum reacted with melanin ; the globulin from malaria-free serum did not. *N. W.*

Henry (A. F. X.). Hémozoïne artificielle (hémomélanine) et paludofloculation. [**Artificial Melanin and Flocculation in Malaria.**]—*Arch. Inst. Prophylactique.* 1939. Vol. 11. No. 3. pp. 211–216.

Dauncey (Kingsley E. D.). **Intramuscular Quinine for Malaria.** [Correspondence.]—*Brit. Med. Jl.* 1941. Mar. 29. p. 494.

Experience in Bihar, India, has made the writer of this letter an advocate for the intramuscular injection of quinine in the treatment of malaria. The site for injection selected by him is the upper part of the middle third of the outer aspect of the thigh : here one can feel the needle pierce the fascia lata. The importance of timing the injections is stressed : the most effective time to give an injection is from one hour to half an hour before the temperature begins to rise. The

aim should be to get the maximum concentration of quinine in the blood when the merozoites are scattered in the blood stream. One timed injection of five grains of quinine is sufficient to cure the acute symptoms. By this form of medication a large amount of quinine might be saved and patients spared the unpleasant effects resulting from the heroic doses of quinine that are still sometimes given.

N. W.

CONDORELLI (Luigi). Porpora emorragica chininica da malaria. (Considerazioni patogenetiche sulla porpora da malaria.) [**Quinine Purpura Haemorrhagica in Malaria: Pathogenesis of Malarial Purpura.**]—*Riv. di Malariologia.* Sez. I. 1941. Jan.–Feb. Vol. 20. No. 1. pp. 8–29. With 5 charts. [15 refs.] English summary (5 lines).

A man aged 27 was serving in Abyssinia in 1935. For a time he was given prophylactic quinine daily and showed no sign of intolerance to the drug. In spite of the drug he fell ill with malaria. The attack was not severe but was accompanied by profuse epistaxis and a generalized petechial rash; he made a rapid recovery after treatment in which quinine had no part. In 1936 he was repatriated to Italy; he was in good health till November 1939 and then fell ill with malaria. It was a sharp attack; the temperature rose to 104°F. and remained at this level for 48 hours. There were no haemorrhagic phenomena. After two days' remission another febrile paroxysm occurred; he was given an injection of 1 gm. of quinine. Half an hour later with intense shivering and a still further rise of temperature there were profuse epistaxis, bleeding from the gums, a diffuse petechial rash all over the body, intense subconjunctival haemorrhage in both eyes, intense haematuria, and a large haematoma at the site of the injection. The symptoms and fever persisted, and six days later the patient was admitted to hospital very dangerously ill. He eventually recovered. The author took full advantage of an interesting case, and the results of the numerous haematological examinations made at the different stages of the patient's illness are set out at length. When the haemorrhagic symptoms and signs had cleared up an injection of 0·5 gm. of quinine caused their return, together with a rise of temperature. A month later a similar dose of quinine caused a slight rise of temperature but no haemorrhagic symptoms. Two and a half months later quinine caused a slight chill but no rise of temperature and no haemorrhagic symptoms. In this case it was clear that quinine and malaria conjointly were responsible for the haemorrhagic phenomena.

The author discusses at great length the pathogenesis of his case and the literature of both malarial and quinine haemorrhagic syndromes.

N. W.

SIEGENBEEK VAN HEUKELOM (A.) & WAHAB. Thrombopenische purpura door idiosyncrasie voor kinine. [**Thrombopenic Purpura due to Quinine Idiosyncrasy.**]—*Geneesk. Tijdschr. v. Nederl-Indië.* 1941. Apr. 29. Vol. 81. No. 17. pp. 906–916. With 1 chart. [34 refs.] English summary.

"Description of thrombopenic purpura caused by chinin in a Chinese boy 17 years old. First attack at home after use of 1400 milligram

sulfas chinini, no malaria ; severe bleeding from the mouth and subcutaneous, lasting three days with practically total disappearance of platelets. Second attack at home also, after 400 mg., again lasting three days, platelets 7000. Third attack experimentally induced in hospital by 200 mg. by mouth, lasting two days with complete disappearance of platelets and shocklike symptoms. Reduction of platelets to 25,000 after 10 mg. by mouth, no bleeding. Other blood values were normal, the spleen was not enlarged.

" During the first experiment the bleeding started one hour and a half after administration of chinin 200 mg., platelets dropping from 540,000 to 28,000 within two hours and a half, completely disappearing in 24 hours. During recovery from the first and second attack the platelet rate rose above normal value.

" Attention is drawn to the fact, that each time hemorrhage stopped some days before the platelet curve showed any sign of recovery. As pointed out by other authors hemorrhage may start with platelets exceeding 50,000. It may be absent with platelets below 10,000, or even during total disappearance of platelets from the blood."

NIVEN (J. C.). **Mapharside in the Treatment of Malaria.**—*Bull. Inst. Med. Res. Federated Malay States.* 1940. No. 6. 8 pp.

Mapharside (mapharsen in America) is a trivalent arsenical preparation, meta-amino-para-hydroxy phenylarsine oxide hydrochloride. Previous reports have stressed its value in the treatment of *P. vivax* infections, mostly in therapeutic malaria. The present communication describes the results of the treatment of 20 *falciparum*, 9 *malariae* and 20 *vivax* infections with mapharside, an equal number of " control " cases of *falciparum* and *vivax* infections being treated with quinine. Parasite counts were made each day from the start of treatment. The mapharside treatment consisted in the administration of two intravenous injections, with an interval of from five to seven days, of 0·04 and 0·06 gm. respectively.

In *vivax* malaria the effect on the parasites was strikingly rapid, much more rapid than that of quinine given by mouth in daily doses of 1·0 gm. per 100 pounds body weight. Against *P. falciparum* and *P. malariae* mapharside is useless ; it has no effect on either schizonts or gametocytes. The author concludes that the place of mapharside in the treatment of malaria will be limited to the treatment of therapeutic *vivax* infections. Further evidence is desirable, however, regarding its value in the treatment of chronic relapsing *vivax* malaria.

N. W.

FEDERATED MALAY STATES. **Annual Report of the Malaria Advisory Board for the Year 1940** [KINGSBURY (A. Neave), Chairman].—30 pp. 1941. Kuala Lumpur. Govt. Press. [$1 or 2*s.* 4*d.*]

As usual this annual report contains much of interest. The year 1940 was another bad malaria year ; the number of malaria cases treated in Government and Estate hospitals in the F.M.S. was 49,000, as compared with 49,700 in 1939. Though the totals are so similar the monthly distribution of cases in the two years was vastly different. In 1940 the prevalence of malaria in May and June throughout the F.M.S. was higher than in those months of any other year since records were kept by the Board. Fortunately there was a decline in incidence

in July and a complete absence of any autumn wave in all four States. The case mortality rate increased from 1·8 per cent. in 1939 to 2·2. Eighty-eight cases of blackwater fever were recorded with 19 deaths.

The preparation M3 of the State Biochemical Institute of Milan was tried as a prophylactic against malaria and found wanting. An Indian preparation " alebrin " was tried in the treatment of 3 cases ; it was much less efficient than quinine. An anti-larval preparation " Cooper's Anti-Malarial Fluid " was found to be less effective and more costly than Malariol, a standard anti-larval oiling mixture.

The control of rural malaria received increased attention during the year. The investigation of conditions in selected *kampongs* was carried out and experimental larval control was being commenced. Details are given of a survey of the Ulu Jempol valley of the Kuala Pilah District of Negri Sembilan. Here the crude spleen rate of children was 33 per cent. *A. philippinensis* is the predominant anopheline. Other *Anopheles* species that are fairly common are *barbirostris*, *hyrcanus*, *kochi* and *aconitus*. Only for short periods were larvae of *A. maculatus* and *A. karwari* at all plentiful. The only mosquito found infected was one *A. maculatus*. The ravines are not properly drained and have swampy floors. It is proposed to construct a series of fish ponds by building dams across the ravines and to treat the seepages by fascine drainage. One advantage of this measure should be an increase in the protein content of the peasant's diet.

In Perak observations were commenced in Berambang Panjang, a small *kampong* in the Bagan Datoh peninsula, near the upstream limit of *A. sundaicus* breeding. The first experimental measure to be tried will be the gradual filling of redundant drains with coconut fronds and other débris.

In Selangor, *kampongs* are under observation with a view to experimental larval control in a wide variety of conditions. The anopheline vectors concerned are *A. barbirostris*, *A. maculatus* and *A. umbrosus*.

Attention is once more directed to the part that has been played by the planting and replanting of rubber estates in determining the increased prevalence of malaria that has characterized the last three years. The soil disturbance affords ideal conditions for the reproduction of *A. maculatus*. Amendments to the Anti-Malarial Enactment have been proposed with a view to diminishing the danger.

Proposals received from Government for the reconstitution of the Malaria Advisory Board, F.M.S., as a Malayan Board, were approved.

N. W.

COVELL (G.). **Antimalaria Operations in Delhi. Part III.**—*Jl. Malaria Inst. of India.* 1941. June. Vol. 4. No. 1. pp. 1–13. With 3 maps, & 28 figs. on 14 plates.

The two previous parts of this report on antimalaria operations in Delhi gave a history of malaria in Delhi and described the distribution and intensity of malaria infection in different parts of the area in 1936, and the recurrent measures that are being taken to control the disease [this *Bulletin*, 1939, Vol. 36, p. 917 ; 1940, Vol. 37, p. 747]. This last communication describes the permanent antimalaria engineering works carried out in the Delhi urban area since 1936. It is an impressive recital. The cost of work already completed is £113,000. Draining, filling and levelling on a very large scale have all been designed to prevent flooding of any area in inhabited parts of the town or

within at least half a mile from them. This aim appears to have been successfully attained. Twenty-eight photographs and three maps make the description easy to follow. The report will be read with special interest by those who have some knowledge of conditions in and around Delhi before this work was put in hand. It is gratifying to learn that the Director of the Malaria Institute of India is a member of the recently formed committee which has the task of co-ordinating the activities of the various authorities concerned with the development of New Delhi and its surroundings. *N. W.*

Chopra (R. N.), Roy (D. N.) & Ghosh (S. M.). **The Insecticidal and Larvicidal Action of the Essential Oils of *Ocimum basilicum* (Linn.) and *Ocimum sanctum* (Linn.).**—*Jl. Malaria Inst. of India.* 1941. June. Vol. 4. No. 1. pp. 109–112.

Ocimum grows wild throughout India, Burma and Ceylon. Parts of the plant are much used in India for the treatment of various diseases, notably bronchitis. The leaves are burnt on cow-dung to repel mosquitoes. Such beneficial properties as Ocimum possesses are generally ascribed to essential oils which different species contain in varying amount. The essential oils of *O. basilicum* and of two varieties of *O. sanctum* (holy basil) were investigated. Both possess some insecticidal action in the case of mosquitoes but such action cannot be compared with that of pyrethrum. The mosquito repellent action of the oil lasts for about two hours. Dried leaves burnt on cow-dung are no more deterrent to mosquitoes than cow-dung burnt alone. The oils of both species possess mosquito larvicidal properties but the high cost of production would prevent their use as larvicides. *N. W.*

Ross (G. R.) & Aylen (D.). **Erosion and Malaria. Measures which Control Both Evils.**—*Rhodesian Agric. Jl.* 1941. Vol. 38. No. 4. pp. 173–191. With 9 plates. [Summarized in *Rev. Applied Entom.* Ser. B. 1941. Oct. Vol. 29. Pt. 10. p. 164.]

"The breeding places of *Anopheles gambiae*, Giles, and *A. funestus*, Giles, the vectors of malaria in Southern Rhodesia, are briefly described, and it is pointed out that, directly or indirectly, a very large proportion of them are provided by erosion. In such cases, the best methods of controlling malaria are those designed to prevent the erosion. This paper deals principally with the types of erosion and ponding likely to occur within a radius of half a mile of dwellings, where the elimination of breeding places is most important. A comprehensive plan is given, based on the requirements of a hypothetical farm presenting all the problems likely to be met with. It comprises the making of storm drains above the area, the replacement of any eroding drain by a grassed channel, the provision of drains round the house and in garden, stock-yards and compound, road drainage, planting of bare areas and drains, making up the ground round water troughs and at gates, and protection work in minor gullies. The low cost of such measures as compared with that of temporary ones is emphasised. The nature of minor gully erosion, the design and lay-out of drains, the planting of couch grass on bare areas, the laying out of roads and their drainage, the treatment of small streams, the control of gully erosion and the treatment of banks of large gullies are dealt with in fair detail, and a list is given of trees that may be used to dry up moist soil."

Hewitt (Redginal) & Kotcher (Emil). **Observations on Household Anophelism in a Selected Group of Mosquito-Proofed and Non-Mosquito-Proofed Homes.**—*Public Health Rep.* 1941. May 16. Vol. 56. No. 20. pp. 1055–1061. With 1 fig.

The observations were made in the Tennessee Valley in the summer of 1940. Houses, both mosquito-proofed and non-proofed, were searched for *A. quadrimaculatus* on three consecutive days of each week from June 1st to August 31st. In June few were found in the houses and the differences between the proofed and non-proofed houses were slight; in July and especially in August, more were found in the non-proofed than in the proofed houses.

Stained mosquitoes were released in the houses, but it was found that few could be recovered on the following day from either group of houses; the presence of mosquito proofing, therefore, does not appear to reduce the number of mosquitoes able to leave the houses. There was little observed flight of stained mosquitoes between houses and barns.

C. W.

Watson (Robert Briggs) & Maher (Helen C.). **An Evaluation of Mosquito-Proofing for Malaria Control based on One Year's Observations.**—*Amer. Jl. Hyg.* 1941. Sept. Vol. 34. No. 2. Sect. C. pp. 86–94. With 2 charts.

This is the first report of an attempt to demonstrate quantitatively the value of mosquito-proofing as an adjunct to other measures of malaria control. The studies were carried out close to Lake Wheeler in the Tennessee Valley which produces *A. quadrimaculatus* in large numbers. The area is populated mostly by tenant farmers. Most of the houses were owned by non-resident landlords who decided whether or not they would allow their houses to be mosquito-proofed. The data presented concern 98 houses mosquito-proofed and 45 not so protected. The population concerned represents a fair sample of the tenant farmers of North Alabama, both negro and white.

All families in the area were visited in April, before the beginning of the transmission season, and blood films were made to estimate the prevalence of residual malaria. Blood films from the total population were also taken in August and in October. Each house was visited once every 10 to 14 days throughout the season of transmission and information collected regarding the incidence of fever suggestive of malaria. Three measures of malaria prevalence were used, a blood index, a primary attack rate, and a total morbidity rate. The primary attack rate is the ratio of cases reported for the first time per 1,000 days of exposure. The days of exposure were accumulated for each individual from May 15th to date of appearance of symptoms or to the end of period of observation, September 30th. The total morbidity rate is the ratio of cases of malaria reported each month, without regard to date of onset, per 1,000 days of exposure.

The blood surveys showed that the parasite indices of persons living in unscreened houses rose during the transmission season, while those of persons living in screened houses remained constant. The primary attack rate for persons in screened houses was 1·64 cases of malaria per 1,000 days of exposure; for persons in unscreened houses, 3·10. The rapid increase of infections in June among white people was not experienced by negroes: negroes possess a considerable relative tolerance for *P. vivax* infections. The peak incidence of malaria in the white

group occurred in June ; in the negro group in August. It would appear that mosquito-proofing gave very considerable protection against malaria infection. *N. W.*

KIKER (Calvin C.) & BREEDLOVE (H. E.). **Mosquito-Proofing for Malaria Control from the Standpoint of Construction Costs.**—*Amer. Jl. Hyg.* 1941. Sept. Vol. 34. No. 2. Sect. C. pp. 95–101. With 4 figs.

In areas bordering on Lake Wheeler in the Tennessee Valley 344 houses were mosquito-proofed at an average cost of $33 per house. Many of the tenant farmer's homes are very dilapidated and mosquito-proofing was sometimes a complicated task. A description is given of the methods employed. The work is too recent to afford data of maintenance costs. *N. W.*

DE NEGRI (Ugo). Rapporti fra iponutrizione e malaria nel Delta del Po. Asili Refettori per bambini malarici. [**Relation between Malnutrition and Malaria in the Po Delta. Feeding Centres for Malarial Children.**]—*Riv. di Malariologia.* Sez. I. 1941. Jan.–Feb. Vol. 20. No. 1. pp. 30–50. With 4 figs., 1 map & 1 chart. French summary (9 lines).

The author has made a study of the diet of the working agricultural population of the Rovigo province in the Delta of the Po and has brought to light the quantitative and qualitative insufficiency of that diet. Details are given of the diet of two representative families. Malaria is rife among these communities, and one can readily accept the author's contention that dietetic insufficiency plays no small part in lowering resistance to malarial and other infections. The altogether insufficient quantity of milk available is specially detrimental to the children. A description is then given of seven feeding centres where children, mostly of preschool age, can pass the day, and of the noteworthy change for the better in the health and general condition of the children benefited. Infected children receive appropriate treatment. [The Provincial Antimalaria Committee of Rovigo is to be congratulated on its initiative in one important aspect of malaria control that has been much neglected in many malaria districts of Southern Europe.] *N. W.*

EJERCITO (Antonio) & CELIS (Espiridion B.). **Another Design of Automatic Siphon Sluice in Malaria Control. (Design II.)**—*Riv. di Malariologia.* Sez. I. 1941. Jan.–Feb. Vol. 20. No. 1. pp. 51–65. With 10 text figs., 1 sketch map & plan on 2 folding plates, & 16 figs. on 4 plates.

The automatic siphon is for a stream of considerable size. A cement culvert pipe, 1 metre in diameter, is placed end up on either side of a concrete dam built from bank to bank of the stream. The distal pipe is set 12 cm. lower than the proximal pipe. They are supported on blocks and fixed to the dam or retaining wall. A cement dome-shaped roof completely closes the upper ends of the pipes, thus forming the siphon. The top of the dome is perforated to receive an iron pipe through which air passes from, or into, the siphon.

The report is very copiously illustrated with photographs and working drawings which are for the most part self-explanatory. It must be confessed that the letterpress does not add to their elucidation.

N. W.

Raffaele (G.). Ulteriori ricerche sulla fase monogonica primaria dei plasmodidi nell'uomo e negli uccelli. [**Further Researches on the Primary Monogonic Phase of Plasmodia in Man and in Birds.**]—*Riv. di Malariologia.* Sez. I. 1940. Vol. 19. No. 4. pp. 193–225. With 1 fig. & 2 plates (1 coloured). [53 refs.] English summary.

The author discusses exoerythrocytic schizonts and states that it has now been definitely established that they originate from sporozoites or from merozoites formed from non-pigmented schizonts within endothelial cells. It is claimed that merozoites formed within red blood corpuscles from pigmented schizonts are unable to give rise to exoerythrocytic schizonts. The fact that they may follow inoculation of blood containing the pigmented stages is due to unrecognized exoerythrocytic merozoites present in the blood inoculated. In a coloured plate is depicted a series of exoerythrocytic schizonts from cases of human malarial infection. One schizont is from the bone marrow of a case of *P. falciparum* infection and two from the bone marrow of a case of *P. malariae* infection. This is the first record of these forms in quartan malaria. A large part of the paper is devoted to a review of present knowledge of this phase of development of malarial parasites, chiefly those of birds. In the text the author gives a diagrammatic representation of what he considers to be the life-history of a malarial parasite.

C. M. W.

Brug (S. L.). Exo-Erythrozytäre Malariaparasiten beim Menschen. [**Exoerythrocytic Malaria Parasites in Man.**]—*Riv. di Malariologia.* Sez. I. 1940. Vol. 19. No. 4. pp. 226–229. With 1 plate & 1 chart.

In lung smears made post mortem from a case of induced malaria in a paralytic, the author noted certain appearances which he interpreted as due to exoerythrocytic schizonts within endothelial cells. In one cell was a round blue body with four chromatin masses. It was devoid of pigment and was regarded as a four-nucleated schizont. In two other cells were as many as forty small, red-staining patches or areas which are considered to be nuclei, some of them in process of multiplication, as there was a tendency to a paired arrangement. It is supposed that these represent schizonts on the way to merozoite production. In the cytoplasm of other cells are numerous rounded reddish bodies or granules, which are described as Rickettsia-like. The various cells are shown in a coloured plate, but apart from the first form noted it seems doubtful if the interpretation placed upon them is correct. Even the first form, which is a body of definite structure, might be interpreted differently.

C. M. W.

BLACKWATER FEVER.

VINT (F. W.). **Some Recent Researches on the Spleen and their Possible Relationship to Blackwater Fever.**—*East African Med. Jl.* 1941. Sept. Vol. 18. No. 6. pp. 162–174. [30 refs.]

In this paper the author gives a brief summary of recent work on the spleen and blood, and then proceeds to discuss their possible bearing on the mechanism of blackwater fever. The circulation of the spleen has been the subject of much controversy. The splenic artery is noteworthy for its large calibre in proportion to its size, while the splenic vein is one of the few veins devoid of valves. It has been calculated that the spleen contributes one-fifth of the total portal blood. The arteries, having been carried down into the splenic pulp by the fibrous trabeculae of the capsule, soon divide and the smaller arteries become surrounded by lymphoid tissue which swells out in places to form Malpighian corpuscles. There is some doubt how these arterioles terminate. It has been thought that some end blindly and discharge their blood into the pulp, while others run into the venous sinuses. Those ending in the venous sinuses (the penicelli) are furnished with peculiar structures (ellipsoids) which are supposed to act as potential valves and prevent backflow. The venous sinus is an unusual structure, being surrounded with barrel-like hoops enclosing fenestrated staves. Arising from the venous sinuses are the venules and their walls have openings called stigmata.

MCNEE (1931) believes that the circulation of the blood in the splenic pulp is two-fold : (*a*) direct, the blood flowing through the arterioles, the venous sinuses, the venules and then into the splenic vein ; (*b*) intermittent, brought about by the contraction and enlargement of the spleen, which consists in emptying the pulp spaces through the stigmata in the walls of the venules and filling again through lateral channels in the walls of the ellipsoids ; the blood can remain stationary in the pulp separated from the general circulation for considerable periods.

KNISELY (1934) has introduced a new conception of splenic circulation. He used a microscope on living, exposed, trans-illuminated spleens of mice, rats and cats, and found that the sinuses and blood vessels were continuous, neither open nor blind ends being found in any blood vessel traced. The blood passes by long straight capillaries to the venous sinuses, its flow being controlled by sphincter-like segments of the arterial tree. The efferent end of the venous sinus contracts tightly and the sinus fills. The plasma filters out through the fenestrae in the walls, leaving the red cells behind. This continues until the sinus is distended 20 to 50 times its normal size with tightly packed red cells. The plasma returns to the circulation through the stigmata in the walls of the venules, but the red cells remain packed in the sinus for periods varying from 10 minutes to several hours. Then the efferent end of the sinus suddenly opens and the packed red cells are discharged in masses. When the sinus has returned to its normal size, blood is conducted as in an ordinary blood vessel for a period. Exercise, fright or adrenalin causes contraction of the spleen and, emptying of the sinuses. If the animal is killed during the observations, disappearances of the vessel walls can be seen during the agonal period with rapid diapedesis of the red cells into the pulp. There some phagocytosis of the cells takes place, thus producing the picture usually seen under the microscope, which has led to so much misunderstanding.

Vint next turns to the question of the storage and destruction of red blood cells in the spleen. Barcroft (1925) found that an increase of external temperature causes not only an increase in the amount of circulating blood but also an increase in the number of red cells and the amount of haemoglobin, and he proved that the increase was accounted for by the release of red blood corpuscles stored in the spleen. In man, the spleen is only 0·25 per cent. of the body weight, yet Barcroft found that the spleen may add 100 cc. of corpuscles to the circulation. It would appear that Barcroft's findings can be explained by Knisely's work on the anatomy of the spleen, the contraction of the organ emptying the venous sinuses of packed red cells and the sinuses thereafter acting as normally conducting blood channels.

Recently, some doubt has been cast on the theory that the spleen is responsible for the destruction of effete red blood cells. Various calculations suggest that in the neighbourhood of two billion red cells are destroyed every minute in the body. If these were being destroyed in the spleen by the endothelial cells it should be relatively easy to demonstrate erythrocytes in the endothelial cells. Vint has recently examined microscopically specimens from 105 spleens and in only two was he able to demonstrate phagocytosis satisfactorily.

Recently Fahraeus (1939) has made a number of interesting observations on the blood. If citrated or defibrinated blood is kept at body temperature, it undergoes rouleaux formation and sediments. If this sedimented blood is shaken up, the sedimentation rate is reduced, rouleaux formation is diminished and the erythrocytes tend to become globular in formation. Fahraeus has called these changes stabilization. Stabilization is probably due to some substance formed in the separated blood during warming and then adsorbed on to the surface of the red cell, because if a specimen of stabilized blood is centrifuged and fresh cells added to the plasma, the reconstituted blood behaves normally.

According to Knisely's conception of the splenic circulation, the blood in the sinuses is separated just as in Fahraeus's experiments. In both cases the blood is kept at body temperature and the reunion of the cells and plasma in the splenic vein corresponds to the shaking up of the blood in the test tube. Consequently, the blood in the splenic vein should be stabilized. In point of fact, various observations indicate that this is the case. Hammarsten (1883) showed that the splenic blood cells were less flattened and showed less rouleaux formation than did arterial blood. This observation was confirmed by other workers and it was also noticed that the splenic blood had a slower sedimentation rate than arterial blood. Fahraeus concludes that prehaemolytic properties are given to the blood's main components by their separation in the spleen, and that haemolysis takes place when they unite in the splenic vein, and not in the spleen itself, as is generally believed.

Turning to blackwater fever, Vint points out that the disease is more frequent amongst Europeans than natives, despite the fact that debility, bad food, dysentery and other infections are predisposing causes. It would appear that it is just these infections which prevent the onset of blackwater. Throughout the years these diseases have caused chronic enlargement of the spleen, resulting in an overgrowth of fibrous tissue which actually destroys the reservoir and separator function of the organ and prevents congestive splenomegaly when an attack of malaria does occur. Vint found that the average weight of spleens from patients not dying of malaria was 13·8 ounces and in cases dying of malaria 13·5 ounces. In the native child, fibrosis of the spleen

has not had time to develop, and therefore an attack of malaria causes enlargement of the organ, with increased separation of the blood and increased haemolysis with a greater drop in the total blood count than would occur in adult natives with fibrosed spleens. The average red cell count in native children suffering from malaria was 2,659,160. In fifty consecutive counts on native adults suffering from malaria, the average count was 4,009,800. According to Fahraeus's researches, various factors are involved in the production of blackwater. These are :—

(1) The degree of separation of the red blood corpuscles and plasma in the splenic sinuses,
(2) The number of red cells in the circulating blood,
(3) The fragility of the red cells,
(4) Toxins present,
(5) Toxicity of medicines administered, and
(6) Susceptibility of the patient.

Biliousness is a common prelude to the onset of blackwater fever. In a normal person it requires 17 cc. of laked red cells before the threshold level of the kidneys is reached and haemoglobin appears in the urine. In a case of blackwater, haemolysis has been going on for some time in the splenic vein before this concentration is reached in the circulating blood, and so the liver has been dealing with the ever-increasing amount of haemoglobin and with the detritus of the broken-down cells. This results in an overworked and overloaded liver and biliousness.

Spherocytosis.—This was seen in blood films during an attack of blackwater and is accompanied by " ghost cells." The latter are the remains of broken-down red cells which have escaped the reticulo-endothelial cells in the liver while the spherocytosis is an indication of the stabilization of the blood in the splenic vein.

Disappearance of malaria parasites.—The explanation appears to be that the infected red cells are already damaged and therefore are the first to undergo stabilization and haemolysis in the splenic vein.

The paper ends with a discussion on the quinine factor in blackwater fever, from which the author concludes that although quinine has no effect on the average normal person, nevertheless when it comes to act on an anaemic stabilized blood in the splenic vein which is in a state of delicate equilibrium between the ordinary haemolysis of effete red cells and the mass haemolysis of blackwater, then it is the deciding factor in the onset of an attack of blackwater fever.

[This is an interesting and suggestive paper. While no doubt many of the theories are open to criticism, the paper is well worth reading for the excellent summary the author gives of modern work on the anatomy and circulation of the spleen and of the stabilization of blood.] *W. Yorke.*

Foy (Henry), Kondi (Athena) & Moumjidis (Aristotelis). **Transfusion of Blackwater Fever Blood into a Normal Individual during Haemolytic Crisis.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1941. Sept. 9. Vol. 35. No. 2. pp. 119–123.

In a previous paper, Foy and Kondi [this *Bulletin*, 1937, Vol. 34, p. 838] recorded the results of injecting blackwater fever blood, taken after varying intervals from the first passage of black urine, into

lunatics. In all, 106 lunatics were injected from 58 cases of blackwater fever. Some of them developed malaria, but in not a single case did blackwater fever develop, although the lunatics were observed for 9 to 18 months. There were certain questions which these experiments did not clear up, *e.g.*, whether blackwater fever patients possessed red blood cells particularly liable to haemolysis by specific auto-haemolysins, or whether blackwater fever patients could haemolyse cells of normal individuals if these were transfused into them. The present paper records an attempt to answer both these questions by means of direct transfusions during haemolytic crises.

Details are given of a severe case of blackwater fever. The patient was a woman, 24 years old. She was admitted to hospital on the 24th September, 1940, with blackwater fever. She stated that on the 22nd September she felt out of sorts and was given an intramuscular injection of quinine bihydrochloride at noon. At midnight she passed black urine; the black urine continued during the 23rd, and on admission to hospital on the 24th she was very icteric, with an enlarged liver and spleen, and was obviously very gravely ill. The urine was black, acid and contained oxy- and met-haemoglobin.

During the 25th September, the patient passed 2,100 cc. of black urine. On the 26th, she was much worse, vomiting, comatose and incontinent. The red cell count had fallen to 756,000; the urine was copious, black and acid. As the patient was still haemolysing and passing plenty of urine, it was decided to transfuse her, and she was given 300 cc. of citrated whole blood at 11.30 a.m. by means of a Tzanck apparatus. By reversing the apparatus, the donor was first given 25 cc. of blood from the blackwater fever patient. The apparatus was then again reversed and the transfusion carried out without a hitch. Three hours after the transfusion, the patient's red cell count was 1,316,000.

On September 27th, the patient continued to pass black urine in large quantities. On September 28th, the red cell count had fallen to 836,000, and as she was still passing a quantity of black urine, another transfusion of 300 cc. was given. Three hours later, the red cell count was 1,296,000. On the 29th and 30th September the haemolysis continued and the patient passed large quantities of black urine. As on the latter date the red cell count had fallen to 840,000, a third transfusion of 300 cc. was given. Three hours later the red cell count had risen to 1,346,000. During the following four days the urine gradually cleared, but on October 4th the red cell count was down to 843,000 and the reticulocytes were 15 per cent. On October 7th, the red cell count was 1,200,000, with 26 per cent. of reticulocytes. The urine was free from all trace of haemoglobin, but loaded with trichomonads. Thereafter the patient made a slow but uneventful recovery.

The history of the man who was given the 25 cc. of the patient's blood on September 16th is as follows: There was nothing to report until October 5th, when he went down with a smart attack of fever, his blood containing *P. falciparum*. He was given 1 gm. of quinine bihydrochloride intramuscularly. The next day his temperature had fallen to normal, but he was given 2 gm. of quinine again intramuscularly. On October 7th, his temperature was again up to 39°C. and parasites were still present in the peripheral blood. Quinine was continued until he had been given 8 gm., and thereafter atebrin was administered. The patient made an uneventful recovery.

The only point noted was that the parasites appeared to be very resistant, both to quinine and atebrin, as the patient was still running a fever with a few parasites in his blood after 8 gm. of quinine and 1gm. of atebrin.

The authors summarize their observations as follows :—

" From the transfusion of blackwater fever blood into a normal healthy adult with a previous history of malaria, it would appear that there are no specific parasites or haemolytic strains of malaria concerned in the genesis of blackwater fever, since the recipient of haemolysing blackwater fever blood failed to develop blackwater fever, or any other sign of haemolysis, although he went down with malignant tertian malaria 11 days after he received the blackwater fever blood. The possibility of his having been infected from other sources was absolutely excluded.

" The fact that the man failed to show any sign of haemolysis, although haemolysins were present in the blood he received, may have been due to the fact that he received insufficient blood ; or that he dealt with any haemolysin he received immediately.

" Blood cells transfused from three normal individuals into a haemolysing case of blackwater fever underwent rapid haemolysis, showing that the red cells of normal individuals are just as susceptible to haemolysis when transfused into blackwater fever patients, as are the blackwater patient's own cells. This fact seems to us to dispose of the view sometimes put forward that the red blood cells of blackwater fever patients are more susceptible to haemolysis than are normal cells, and makes it appear probable that a circulating haemolysin may be responsible for the trouble. Of course it is by no means improbable that continuous sensitization is necessary before the red cells become liable to haemolysis, or infection over long periods with a special strain of malaria, and that one infection is not sufficient to sensitize the individual.

" Transfusion, even in moribund cases with red cell counts as low as 800,000 per c.mm., is a life-saving measure, provided that renal function is being maintained." W. Y.

Foy (Henry) & Lewis (E. Gaynor). **Blood Transfusion in Blackwater Fever and Haemolytic Anaemias following Sulphonamide Therapy.** —*South African Digest of War Medicine.* 1941. Dec. Vol. 1. No. 6. pp. 137–143. With 2 charts.

The authors consider that a certain amount of prejudice exists against blood transfusion in blackwater fever and in the haemolytic anaemias following sulphonamide therapy, and that this prejudice is based on the belief that blood transfusion may aggravate the haemolytic process.

Two graphs are given, the first showing the fluctuation in the haemolytic process (erythrocyte counts and urinary output of haemoglobin and methaemoglobin) in a patient with blackwater fever who was not transfused, and the second somewhat similar fluctuations in a patient who had four transfusions, each of 300 cc. of blood. The authors argue that " from these two cases, which are representative of many similar ones in Salonika, it is evident that the recurring haemolyses are not related to the transfusions but are a characteristic feature of blackwater fever ; their existence should not deter transfusions in all anaemic cases."

The indirect continuous drip method is recommended, as it permits of slow administration, the giving of large doses if necessary, and by combining intravenous glucose and saline, the giving of repeated transfusions without withdrawal of the needle from the vein. Stress is

laid on the necessity for proper grouping and compatibility tests. A blood level of 1·5 to 2·5 millions should be arrived at: 500 cc. of blood raises the erythrocyte count by 500,000 to 600,000 per cmm. A satisfactory rate of administration with doses up to 500 cc. is 40 to 60 drops per minute.

The question whether a patient with blackwater should be moved may have to be considered. In Salonika where the majority of cases have to be moved long distances over very bad roads, and often in the most primitive conveyance, the death rate is no higher than elsewhere (900 cases). Unnecessary movement should be avoided, but if facilities for treatment at the clearing station are not available, then the patient can and should be moved.

The question of fever sometimes arises in cases of blackwater and it will have to be decided whether this is due to malaria parasites or other causes (protein shock, etc.). If due to parasites, these should be dealt with by means of atebrin or quinine. It will frequently be found that a patient will run a fever for a day or two which subsides without any treatment; if, however, fever persists and parasites are present, they should be treated. There is little real evidence that quinine or atebrin given during an attack of blackwater is likely to cause a recurrence of the haemolysis except, of course, in cases of quinine sensitivity.

The authors next stress the importance of keeping up the fluid intake so as to diminish the danger of anuria. At least 2,000 cc. of fluids should be given daily; during vomiting, 1,000 cc. of saline or 5 per cent. glucose repeated every 12 hours should be given intramuscularly or intravenously. When vomiting has stopped, sod. bicarbonate 0·6 gm. (10 grains) should be given orally until the urine is alkaline to litmus.

The paper concludes with the recommendation that blood transfusions should be given to combat the anaemia which sometimes occurs as the result of sulphanilamide treatment. [In general the reviewer is in agreement with the rules laid down in this paper, which as a matter of fact are commonly practised by those who have to deal with blackwater fever. There is, however, one important question upon which present knowledge (or ignorance) hardly warrants dogmatism, *viz.*, should quinine or atebrin be given during an attack of blackwater fever? The usual practice is to withhold these drugs until the patient has recovered from his blackwater and the urine has cleared. The present authors recommend that if fever persists and parasites are present antimalarial treatment should be given. As this advice may be followed by many who have little experience of the disease, as it is contrary to general practice, and as conceivably it may be wrong, it is of interest to examine some of the authors' statements bearing upon it. What exactly do the authors mean when they write "if, however, fever persists and parasites are present they should be treated"? *P. falciparum* is probably always present in the body of an individual suffering from blackwater, but it is general knowledge that it is so scanty in the peripheral blood that it cannot be discovered except at the very commencement of the attack. Again, fever is a constant sign in blackwater and is intimately bound up with the haemolytic paroxysms and not directly related to the presence of a malaria infection. What therefore does the authors' direction mean? Always give quinine or never give it?

Finally, it is no doubt true that "there is little real evidence that quinine or atebrin given during an attack of blackwater is likely to cause a recurrence of the haemolyses except, of course, in cases of

quinine sensitivity," but there is equally little evidence that in certain cases quinine or atebrin given during an attack of blackwater may not aggravate the haemolytic process. The reviewer has frequently given quinine to blackwater fever patients, usually with no obvious effect but sometimes the drug has been followed by a violent haemolytic paroxysm. Whether the latter is a *propter* as well as a *post* phenomenon it is impossible to state, just as it is impossible to forecast which case of malignant tertian malaria will develop an attack of blackwater when he is treated with quinine or atebrin.

On the whole, it seems to the reviewer safer and better to withhold quinine and atebrin until the attack of blackwater is over. The malignant tertian infection in blackwater fever cases is so scanty that its treatment can well be delayed for a few days. The antimalarial drugs can hardly be expected to influence the haemolytic process favourably, and it is possible that in some cases they may influence it in a very unfavourable direction. The plan followed by the reviewer is to withhold quinine during the attack of blackwater (except in the very rare instance when there is a double malaria infection and *P. vivax* is causing trouble) and then when the blackwater is over to give the patient one grain of quinine and gradually to increase the dose on successive days until full doses are reached ; this is, of course, essential, as otherwise the attack of blackwater will probably be followed by a relapse of the malignant tertian malaria.] *W. Y.*

FAIRLEY (N. Hamilton). **Methaemalbumin. Part I. Clinical Aspects.** —*Quarterly Jl. Med.* 1941. Apr. N.S. Vol. 10. No. 38. pp. 95–115. With 1 fig. & 1 plate. [29 refs.]

Most of the work mentioned in this paper has already appeared elsewhere and has been referred to in this *Bulletin*. The following are the summary and conclusions :—

" (1) The spectroscopic appearances and chemical reactions of methaemalbumin in human plasma and when concentrated in the albumin fraction of blackwater fever serum are described.

" (2) Simple chemical methods used in conjunction with a direct vision spectroscope are described which serve to differentiate methaemalbumin from methaemoglobin and sulphaemoglobin.

" (3) Methaemoglobin has been universally described in the plasma of diseases associated with intravascular haemolysis and haemoglobinuria. This error has arisen through failure to differentiate spectroscopically between methaemoglobin and methaemalbumin.

" (4) As methaemoglobin and sulphaemoglobin are essentially confined within the corpuscle it is suggested that the term methaemoglobincythaemia should replace that of methaemoglobinaemia, and sulphaemoglobincythaemia that of sulphaemoglobinaemia.

" (5) Since it has been shown that haematin (ferric) in plasma immediately unites with the serum albumin to form methaemalbumin, Schumm's test in plasma is to be regarded as essentially a test indicating the presence of methaemalbumin, and not free haematin as has previously been supposed.

" (6) It follows that the condition previously described in medical literature as haematinaemia on the basis of this test should henceforth be called methaemalbuminaemia.

" (7) From a biochemical viewpoint the haemolytic anaemias fall naturally into three groups accordingly as they show : (*a*) hyperbilirubinaemia alone, (*b*) hyperbilirubinaemia and methaemalbuminaemia, and (*c*) hyperbilirubinaemia, methaemalbuminaemia, and haemoglobinaemia.

" (8) Regarding the site of haemolysis the available evidence suggests that hyperbilirubinaemia associated with a negative Schumm's test is indicative of intracellular blood destruction, whereas methaemalbuminaemia implies lysis of corpuscles in the circulating blood."

W. Y.

FAIRLEY (N. Hamilton). **Methaemalbumin. Part II. Its Synthesis, Chemical Behaviour and Experimental Production in Man and Monkeys.**—*Quarterly Jl. Med.* 1941. Apr. N.S. Vol. 10. No. 38. pp. 115–138. With 2 figs. [20 refs.]

This paper also contains little that has not previously been published but, as will be seen from the following lengthy summary, the author brings his work on methaemalbumin up to date.

" 1. Methaemalbumin (pseudo-methaemoglobin) is immediately produced by the addition of alkaline haematin (ferric), prepared from pure haemin, to human and simian plasma at 37°C., but not to the plasma of other mammals.

" 2. Methaemalbumin is also formed when alkaline haematin (ferric) is added to the albumin fraction, but not to the euglobulin and pseudoglobulin fractions, of human and simian plasma.

" 3. When alkaline haematin (ferric) is added to the individual proteins contained in the albumin fraction of human serum, crystalbumin, seroglycoid, and globoglycoid, methaemalbumin is formed with crystalbumin only.

" 4. On the reversion spectroscope synthesized methaemalbumin presents a three-banded spectrum composed of an α band situated at 623 $\mu\mu$ to 624 $\mu\mu$, a β band at 540 $\mu\mu$ to 541 $\mu\mu$, and a γ band at 500 $\mu\mu$ to 501 $\mu\mu$, superimposed on a general absorption ; this is identical with the spectrum observed when methaemalbumin is concentrated in the albumin fraction of blackwater-fever plasma.

" 5. The chemical reactions of synthesized methaemalbumin are identical with those observed with methaemalbumin found either in blackwater-fever plasma or concentrated in its albumin fraction.

" 6. On reduction with sodium hydrosulphite, a compound, haemalbumin, with a two-banded spectrum is formed containing ferrous iron; further treatment with carbon monoxide leads to the formation of carboxyhaemalbumin, characterized by a spectrum very similar to that of carboxyhaemoglobin.

" 7. Haemalbumin differs from haemoglobin in not combining loosely with oxygen ; this may be due either to an absence of polymerization or to its possessing a different protein component, albumin instead of globin.

" 8. The effect of changes in pH on the wave length of the α band in various haematin mixtures was investigated.

" 9. An enhanced stability in the presence of acid was demonstrated with human serum-haematin and human serum-albumin-fraction-haematin mixtures compared with colloidal haematin, recrystallized egg-albumin-haematin, and the globulin-fraction-haematin mixtures.

" 10. A similar enhanced stability in the presence of alkali is known to occur ; these data indicate that human serum-albumin is not merely acting as a protective colloid keeping haematin in solution, but is chemically combined with haematin.

" 11. When human albumin-haematin mixtures are examined in the ultra-centrifuge the pigment sediments at the same rate as serum-albumin, whereas in an egg albumin-haematin mixture it sediments in a heterogeneous manner like colloidal haematin. These facts also indicate a firm union of albumin and haematin probably involving a chemical linkage.

" 12. The conclusion reached from this study is that methaemalbumin is a definite chemical compound consisting of a prosthetic group, oxidized haematin (ferric), and a protein component, native serum-albumin.

" 13. In rabbit serum-haematin mixture the spectrum resembles that of alkaline haematin, not methaemalbumin; on the ultra-centrifuge, however, the pigment sediments at the same rate as serum-albumin so that here, also, an albumin-haematin compound is probably formed.

" 14. On injecting alkaline haematin (ferric) intravenously in man in a dosage of 4 mg. per kilo, methaemalbumin and not haematin was found in the plasma, which was brown coloured.

" 15. Methaemalbumin was concentrated in the albumin fraction of such sera, and was found to differ from alkaline haematin both spectroscopically and in its chemical behaviour.

" 16. In both the plasma and the albumin fraction of the serum the α band was situated at 623 μμ, whereas with the original alkaline haematin it was at 616 μμ. Other differences were also demonstrable.

" 17. On the addition of sodium hydrosulphite a double-banded spectrum with an α band at 572 μμ and a β band at 531 μμ was found, owing to the formation of haemalbumin. In the case of alkaline haematin a broad single-banded spectrum is produced under similar conditions.

" 18. Other differences include the stability of methaemalbumin in the presence of alkalis and the formation of carboxyhaemalbumin after treatment with sodium hydrosulphite and carbon monoxide.

" 19. Similar findings are recorded with monkeys of the species *Cercopithicus aethiops*, *Macacus rhesus*, and *Macacus sinicus*.

" 20. In addition, it was found that when reduced alkaline haematin (ferrous) was injected intravenously in these animals, methaemalbumin was formed, indicating that in the blood-stream reduced haematin (ferrous) was immediately oxidized to haematin (ferric) which combined with serum-albumin to form methaemalbumin.

" 21. The bearing of these findings on the katabolism of circulating extra-corpuscular haemoglobin in intravascular haemolysis is discussed."

W. Y.

Fox (Charles L.). **Spectrophotometres of Fairley's New Blood Pigment, Methemalbumin.**—*Jl. Clin. Investigation.* 1941. Sept. Vol. 20. No. 5. pp. 603–606. With 3 figs.

In the course of the study of acute haemolytic anaemia and haemoglobinuria during administration of sulphonamide drugs, the patients' sera were found to contain a pigment which, like methaemoglobin and sulphaemoglobin, showed an absorption in the red region of the spectrum. The characteristic band of this pigment, around λ620 mμ and adjacent to that of methaemoglobin, was not altered by cyanide, although that of methaemoglobin was obliterated. About the same time, Fairley's papers appeared describing a new pigment which became known as methaemalbumin.

In the present work, the author has determined the absorption coefficients of the new pigment. The work is of a somewhat technical nature, and must be consulted in the original by those interested. The following are the conclusions :—

" Fairley's new blood pigment methemalbumin was measured in the visible range with the recording spectrophotometer and preliminary values of its absorption coefficients were obtained.

" The characteristic absorption curve of this new pigment is compared with that of hemoglobin, methemoglobin, and sulfhemoglobin.

" The data obtained are utilized in measuring the formation of methemalbumin, *in vivo* and *in vitro*,

W. Y.

Weise (W.). Ueber Hämatinämie bei Malaria. [**Haematinaemia in Malaria.**]—*Arquivos do Inst. Biol.* Buenos Aires. 1940. Vol. 11. pp. 595–600. [24 refs.]

Schumm (1912) was the first to demonstrate the presence of haematin in human serum in pathological conditions. The spectrum of haematin is very similar to that of methaemoglobin, but the addition of a little soda solution causes the band in the orange to disappear with methaemoglobin, whereas the similar band of haematin persists. Haematinaemia has been found in a whole series of pathological conditions, *viz.*, after certain poisons, such as potassium chlorate, dinitrobenzol, etc., in certain haemolytic conditions, such as pernicious anaemia, paroxysmal haemoglobinuria and in certain other severe conditions such as acute yellow atrophy of the liver. Schumm and Hegler also found haematinaemia in 6 of 11 cases of malaria, and since then it has been frequently found in this disease.

The author considers the source of the haematinaemia in malaria. The pigment of the parasitized red cells consists wholly or in great part of haematin. Heilmeyer has reached the conclusion that the malaria pigment is a combination of haematin and a nitrogen-containing substance. Apparently the malaria parasite breaks up the haemoglobin using the globulin constituent as nourishment and leaving the haematin behind as a combination with the nitrogenous substance. When schizogony occurs, the pigment escapes into the blood plasma and is demonstrable there before it is taken up by the reticulo-endothelial cells. The breaking down of haemoglobin leads, under physiological conditions, to bilirubin. From the chemical standpoint, the change from haematin to bilirubin is very plausible, even though the conversion has not yet been accomplished *in vitro*.

Bilirubin is increased in the serum in malaria. It is iron-free, and the iron-containing fraction is separated off as haemosiderin. In malaria, haemosiderin is found especially in the liver. Further, as it has been shown that there is an increased stercobilin excretion in malaria, it seems reasonable to assume that the conversion and excretion of the malaria pigment take place in the above manner. The correctness of this view, however, became doubtful when Duesberg (1934) showed that injected haematin was not converted into bilirubin. Apparently, then, the biliary pigment must arise directly from haemoglobin and not through the intermediary of haematin. In conclusion, it can be said that the malaria pigment consists of haematin, which is conveyed by the circulation to the organs (liver and spleen) in which the destruction of the blood pigment normally occurs. It is probable that the gradual conversion of the pigment to the biliary pigment takes place while the iron is split off in the form of haemosiderin.

There is a belief amongst malariologists that the number of erythrocytes which are destroyed during a malarial paroxysm is greater than those infected with parasites, and it is, consequently, assumed that the parasitized red cells contain a haemolysin which destroys a number of non-parasitized cells. The author believes that the haemolysis which takes place in blackwater fever differs only in degree from that which occurs habitually in malaria. He remarks that in *Plasmodium knowlesi* infections of monkeys, the haemolytic processes are so pronounced that haemoglobinuria is the rule. [It has always appeared to the reviewer that there is a fundamental difference between the genesis of the haemoglobinuria in blackwater fever of man and in that

which is frequently seen in *P. knowlesi* infection of monkeys. In the former infection, the number of malaria parasites is comparatively small when the attack of blackwater commences, whilst in the latter the haemoglobinuria only occurs at the end of the malaria infection, when the animal is dying with an overwhelming mass of parasites in the blood. In short, the haemoglobinuria in monkey malaria is proportionate to the mass of the infection, just as it is in *Babesia canis* and other Babesia infections, whilst in man the intensity of the haemoglobinuria appears to be quite independent of the intensity of the malaria infection.]

Weise continues by saying that the haemoglobin set free into the plasma is so rapidly removed that the concentration of haemoglobinaemia is low. Haemoglobinaemia is thus a second source of haematin in blood serum. The conversion has been shown by Hamilton Fairley, who has demonstrated in the serum of blackwater fever cases a new pigment closely allied to methaemoglobin. The chemical and spectroscopic behaviour of this new pigment in the serum agrees with that of haematin. Fairley made a very interesting observation when he showed that it was possible to produce the new pigment *in vitro* by incubating human serum with haemoglobin for 24 to 48 hours. Weise has some doubts whether it is necessary to give a special name, methaemalbumin, to a pigment which consists of a combination of haematin and albumin. *W. Y.*

Lui Kwai To. **Report of a Case of Blackwater Fever.**—*Caduceus.* 1941. May. Vol. 20. No. 2. pp. 128–130.

The author points out that three cases of blackwater fever have been reported in the Kowloon Peninsula at Hong Kong during the past two years. He has recently come across a fourth case, and in view of the rarity of the disease in China, he has decided to report it.

A clinical history is given, and details of blood examinations. The points of interest appear to be that the patient was an immigrant to a place where malignant tertian malaria is common, and that there was an interval of five days between the administration of quinine and the appearance of haemoglobinuria, so that it is doubtful whether quinine had precipitated the attack in this case as it had done in previous cases. *W. Y.*

See also p. 279, Robinson, **Favism in Children.**

Bhattacharjee (Jagadish C.). **Blackwater Fever in the Hills.**—*Indian Med. Gaz.* 1941. July. Vol. 76. No. 7. pp. 419–420.

Altschule (Mark D.) & Gilligan (D. Rourke). **Acute, Massive Hemoglobinuria of Obscure Cause, with Jaundice and Anemia. Report of a Case with Clinical and Hematologic Studies and Measurements of the Blood Pigment Metabolism.**—*Arch. Intern. Med.* 1941. Nov. Vol. 68. No. 5. pp. 957–978. With 1 chart. [Refs. in footnotes.]

A clinical account is given of an unusual case of acute, severe haemoglobinuria, accompanied by jaundice and slowly developing anaemia,

with final recovery. The clinical and laboratory findings in this case did not conform completely with those in any recognized type of haemolytic attack leading to haemoglobinuria. The continuance of the haemolytic attack for three weeks gave an unusual opportunity for studying the quantitative aspects of the haemolysis, and many haematological studies were made. The authors summarize their observations as follows :—

" A case of acute, massive hemoglobinemia and hemoglobinuria of obscure cause, in which moderate jaundice and anemia developed, is reported. Hemoglobinemia and hemoglobinuria were greatest during the first days after the onset of the attack and continued for approximately three weeks.

" The red blood cell count decreased during the first two weeks of the attack from 4,710,000 to 2,900,000 and the concentration of hemoglobin in the blood decreased from 94 to 59 per cent. Clinical jaundice increased during the first four days of the attack and then gradually disappeared during the following week.

" The spleen and the liver were enlarged during the attack ; subsequently the size of the spleen decreased slightly. Renal function was reduced during the attack and subsequently returned to normal. Hepatic function was normal.

" Oxyhemoglobin and methemalbumin were identified spectrophotometrically in the plasma. The urinary pigment was chiefly oxyhemoglobin.

" Quantitative studies of the hemoglobin of the plasma and the urine and quantitative studies of the fecal output of urobilinogen revealed the extent of hemolysis during the attack. Calculations based on the values for hemoglobin in the plasma and in the urine indicated hemolysis of the red cells of approximately 1,400 cc. of the patient's blood during the first week of the attack, of 400 cc. during the second week and of 200 cc. during the third.

" Calculations based on excretion of urobilinogen in the stools collected from the fourth to the nineteenth day after the onset of hemoglobinuria indicated hemolysis of approximately 1,000 cc. of blood during this period, as compared with hemolysis of approximately 1,300 cc. for the same period as calculated from the values for plasma hemoglobin.

" The slow development of moderate anemia and moderate jaundice accorded with the amount of blood destruction represented by these calculations. The correspondence between the amounts of blood destroyed during the attack as calculated from the values for plasma hemoglobin and from the total urobilinogen excretion demonstrated that all of the hemoglobin from the blood destroyed during the attack was released into the circulation. This situation is contrasted with that in the hemolytic attacks occurring in some conditions in which more severe anemia develops with greater rapidity and yet in which there may be no evidences of ' intravascular ' hemolysis.

" During the later stages of the hemolytic attack in this patient it was demonstrated that walking caused a definite but slight exacerbation of hemolysis ; after the end of the attack, hemolysis could not be induced by walking or by standing. Exacerbation of hemolysis on walking did not occur in a patient with Marchiafava-Micheli disease with associated hemoglobinemia.

" The clinical manifestations and the laboratory findings in this case were not typical of those in any recognized type of hemolytic attack. No autoagglutinins could be demonstrated in the blood of this patient when tests were made on serum incubated in the cold or at body or room temperature. The fragility of the red cells to hypotonic solutions of sodium chloride was normal. The differential diagnosis of hemoglobinuria is discussed."

W. Y.

YUILE (Charles L.) & CLARK (William F.). **Myohemoglobinuria. A Study of the Renal Clearance of Myohemoglobin in Dogs.**—*Jl. Experim. Med.* 1941. Sept. 1. Vol. 74. No. 3. pp. 187–196. With 3 figs. [14 refs.]

In this work the authors have studied the simultaneous renal clearance of myohaemoglobin and creatinine in the dog. As MONKE and Yuile (1940) have already applied this method to haemoglobin, a quantitative comparison of the renal excretion of the two substances can readily be made. A detailed account is given of the technique and of the experimental observations. These should be consulted in the original by those interested.

The results show that myohaemoglobin is cleared from the plasma about 25 times more rapidly than haemoglobin, but the mode of excretion appears to be similar for the two substances. The following summary is given :—

" When myohemoglobin is injected intravenously into dogs, in amounts ranging from 0·75 to 1·50 gm., it is rapidly eliminated from the plasma and approximately 65 per cent. is excreted by the kidneys in from 1½ to 2½ hours.

" Myohemoglobin does not appear in the urine below a threshold plasma concentration which is slightly under 20 mg. per 100 cc. but above this level the rate of renal excretion is directly proportional to the plasma concentration.

" The maximum myohemoglobin/creatinine clearance ratio averages 0·58 contrasted with a value of 0·023 for blood hemoglobin. This indicates that the rate of renal clearance of myohemoglobin is twenty-five times more rapid than that of blood hemoglobin. Evidence is presented that the excretory mechanism is essentially similar for the two substances but that differences in molecular weight account for different rates of glomerular filtration."

W. Y.

YUILE (Charles L.), STEINMAN (John F.), HAHN (P. F.) & CLARK (William F.). **The Tubular Factor in Renal Hemoglobin Excretion.**—*Jl. Experim. Med.* 1941. Sept. 1. Vol. 74. No. 3. pp. 197–202. With 1 fig.

WHIPPLE (1932) has shown that the renal threshold for haemoglobin in dogs could be markedly lowered by multiple daily injections large enough to cause haemoglobinuria. Histological examination of the epithelium of the convoluted tubules showed dense deposits of iron-staining pigment after repeated injections of haemoglobin, and the lowered thresholds were attributed to a cessation of tubular reabsorption.

In order to obtain further information regarding the rôle of the tubular epithelium in renal haemoglobin elimination, the authors decided to re-examine the phenomenon with the aid of the precise quantitative methods recently used by MONKE and Yuile (1940) to determine the renal clearance of haemoglobin. The following summary of their work is given :—

" A drop has been observed in the renal threshold for hemoglobin in dogs, of over 60 per cent., following repeated injections daily. It was not associated with a cessation of tubular reabsorption.

" Hemoglobin excretion rate curves, obtained initially and after lowering the threshold, have proved to be parallel lines originating at the respective levels,

"Hemoglobin containing radio-active iron has been used to determine the amount of iron retained by the kidneys 24 hours after injection.

"The kidneys of normal animals retain slightly less iron than those of animals with lowered thresholds, despite the fact that the former group has a much higher estimated rate of tubular reabsorption.

"It is suggested that hemoglobin products are more rapidly removed from the kidneys of normal animals, following reabsorption, than from those of animals which have received multiple injections of hemoglobin."

W. Y.

MISCELLANEOUS.

Bulletin of the Health Organisation. (League of Nations.) 1940/41. Vol. 9. No. 3. pp. 247–268. With 1 map.—**The League of Nations Anti-Epidemic Work in China in 1939.**

Early in 1938 three units, each staffed by several European medical men of wide experience, arrived in China under the auspices of the League of Nations. Their functions included the establishment of laboratories, the creation of health services and, in particular, the control of typhus, plague, cholera and smallpox. Malaria was one of the main problems along the China-Burma highway and elsewhere, and was thoroughly investigated, with results which have been reviewed in this *Bulletin*, 1940, Vol. 37, p. 792; 1941, Vol. 38, pp. 103, 501, 502. Some of the details of these investigations are given in the present report.

Cholera broke out in Hunan in 1938 and spread to Yunnan, and many foci were found; about 4,000,000 vaccinations were performed in Hunan. Plague is endemic in the north of Burma among the Shan tribes, and there was a severe outbreak near the Chinese frontier; it is recognized that danger appears to lie along the old caravan routes and the Burma road. Typhus was present in refugees in the north-west, and relapsing fever was also found, especially round the city of Sian where, in the first half of 1938, almost 80 per cent. of the refugee patients admitted to hospital were suffering from that disease.

Endemic goitre is widespread in the mountains of Southern China, and means were devised whereby potassium iodide was incorporated in the native rock salt which constitutes the sole supply of sodium chloride in Yunnan. Potassium iodide was also administered periodically to schoolchildren.

C. W.

War Medicine. Chicago. 1941. July. Vol. 1. No. 4. pp. 539–568.—**Notes on the Treatment and Control of Certain Tropical Diseases. Circular letter No. 56 from the Office of the Surgeon General, War Department, Washington, D.C.**

The diseases dealt with are:—Cholera, dysentery (amoebic and bacillary), filariasis, hookworm infection, leishmaniasis, malaria and blackwater fever, onchocerciasis, oroya fever, pinta, plague, relapsing fever, schistosomiasis, yaws and yellow fever. This alphabetical order is presumably adopted for ease of reference. In each case the geographical distribution is given and brief statements are made concerning the aetiological agents, methods of transmission and diagnosis. The

treatments advised are those in common use, but, as in the cases of sulphaguanidine in bacillary dysentery and sulphathiazole in plague, recent experimental work has not been overlooked. The outlines of preventive measures are included.

The notes are presented in tabular form and are dogmatic in expression ; they should prove to be of great value to medical officers brought for the first time into contact with tropical diseases. *C. W.*

FARRELL (Elliston). **Recent Progress in Tropical Medicine.**—*U. S. Nav. Med. Bull.* 1940. Jan. Vol. 38. No. 1. pp. 80–90. [59 refs.]

GHOSH (R. K.). **A Case of Confluent Smallpox : Treatment—Chemotherapy.**—*Indian Med. Gaz.* 1941. Sept. Vol. 76. No. 9. p. 544. With 1 chart.

The patient had confluent smallpox and was in a highly toxaemic state, with delirium, for a week, though the temperature was not very high. From the fourth day of illness he was given sulphonamide tablets (Albert David) or Dagenan (sulphapyridine), three tablets daily [each presumably of 0·5 gm.] and was discharged cured after a month, the temperature becoming normal in 10 days after this treatment was started. *C. W.*

BRÁS DE SÁ. **An Epidemic of Pemphigus in a Village of Bardez.**—*Arquivos da Escola Méd.-Cirúrg de Nova Goa.* 1938. Ser. A. No. 12. pp. 303–308.

This is an account of an outbreak of 34 cases of a contagious form of pemphigus in a single village ; 10 cases occurred in members of one Hindu family. The incubation period was 10 to 14 days ; there was initial fever to 104°F. with delirium or convulsions (in children). An erythematous rash appeared on the second day, beginning on the face and extending to the body. Within a few hours the rash became papular, vesicular and bullous, the bullae were round or irregular and were not umbilicated ; they are described as being as large as beans. The bullous fluid became seropurulent and if the bulla burst there was left an ulcer which healed in a fortnight, leaving a scar. The rash was generalized and was accompanied by sensations of burning and pain. In non-fatal cases the temperature subsided after the fourth or fifth day, but in the 10 fatal cases death occurred between the fourth and ninth days from bronchopneumonia.

The disease affected children and adults and some of the patients had had smallpox or had been vaccinated. It was definitely a form of pemphigus and smallpox and chickenpox could be excluded. The aetiology is unknown ; attempts to cultivate an organism were unsuccessful, but the author appears to incline to the view that it may be a virus disease. *C. W.*

BROCH (Ole Jacob). Trombopenisk purpura etter kinidin. [**Thrombopenic Purpura after Treatment with Quinidine.**]—*Nordisk Med.* 1941. May 17. Vol. 10. No. 20. 1542–1544. [19 refs.] English summary.

" A 27 year old woman was admitted to the hospital for thrombopenic purpura after taking quinidine for a period of 14 days. During

the preceding half year, she had taken quinidine for 4–5 weeks without having the slightest trouble.

" Definite thrombopenia without any other hematologic symptoms and without morphologic changes of the megakaryocytes in the sternal marrow, was experimentally produced several times by administering 0·40 grams of quinidine sulphate per os. During the course of an hour, the number of thrombocytes sank to about one fifth of their normal value. The lowest value was attained after five hours. The original values were approximately reached after 48 hours.

" In essential thrombopenia, it is a recognized fact that the decrease in the number of blood platelets is brought about by the reticulo-endothelial system. Further details of this mechanism are as yet unknown. It is probable that allergic thrombopenia has a similar mechanism but that no direct effect is exerted on thrombopoiesis. The rapid drop and the rather quick remission favour this belief.

" It is probable that no actual destruction of the blood platelets occurs, but that the blood platelets are only temporarily withheld from the circulation. The reticulo-endothelial system plays a decisive rôle in this process."

ROBINSON (P.). **Favism in Children.**—*Amer. Jl. Dis. Children.* 1941. Oct. Vol. 62. No. 4. pp. 701–707. [17 refs.]

During March, 1939, the author and his colleagues in Palestine came across three children with severe acute haemolytic anaemia of unknown origin. The symptoms and the course of the illness resembled those of Lederer's anaemia, of which about 70 cases, mostly in children, have been recorded from different countries. The course of the present disease is highly dramatic. The onset is sudden, and within a few days, or even hours, during which vomiting is the most striking symptom, a serious state arises which is hard to interpret. The skin is pale grey or yellowish, and eyes are sunken and dull, and consciousness becomes clouded. The urine is brown or red. Examination of the blood shows severe anaemia. The course of recovery is even more remarkable than the onset. The patient, who was apparently dying a short time previously, sits up in bed, asks for food and, apart from being anaemic, seems absolutely normal. The improvement of the blood is steady, but slow ; normal values are found after at least a week. Very few of the patients die.

Details are given regarding one of the author's cases, and the numerous clinico-pathological observations made during several days of illness are summarized in a table.

In March 1940, the three children seen the previous year came under observation again, suffering from the same disease. This disposition to relapse and the marked eosinophilia in the blood and the bone marrow compelled the author to discard his original diagnosis of Lederer's anaemia and to look for another explanation. Various workers have drawn attention to the fact that some patients described as having Lederer's anaemia may in reality have had haemolytic icterus. In the present cases, however, splenomegaly and jaundice were present only during the attacks. The osmotic resistance of the erythrocytes was normal or increased. Spherocytosis was never observed. The bone marrow picture resembled that described by MAINZER and JOEL (1938) in a case of anaemia due to lack of vitamin A.

About the same time that the three original patients came under observation again, a boy of 1½ years, the son of a farmer, was admitted to hospital with uraemic coma. The history was typical of Lederer's anaemia, but the mother mentioned that on the farm broad beans (*Vicia fava*) were being cultivated and that two days before, the child, who liked the blossoms and the beans of the plant very much, had eaten some uncooked beans. This recalled to the author's mind the condition known in Italy and Greece as favism. Favism is an acute haemolytic anaemia due to the ingestion of broad beans and has been known for centuries in the Mediterranean region. The disease is said to be especially common in Sardinia and Sicily. Besides the haemolytic anaemia, which is the severest form of the disease, there may also be other conditions due to the same cause, such as fainting, vomiting or diarrhoea. The morbidity rate in Sardinia is as high as 5·17 per cent., with a case mortality rate of 8 per cent. Only two cases have been reported in the United States, and the disease has never before been observed in Palestine. According to HUTTON, the factor of heredity is of importance in 20 per cent. of cases.

On going back into the history of his cases, Robinson found that all of the first three patients, whom he considered to be suffering from Lederer's anaemia, had fallen ill, both the first and the second times, one or two days after eating broad beans. He was unable to trace two other patients seen in 1939, but in August 1940, a 12-year-old boy, and in January 1941, a 7-year-old boy, were admitted to hospital with acute haemolytic anaemia, a day after they had eaten broad beans. Both of them survived. Robinson writes that it is remarkable that at least three of his patients were particularly fond of broad beans.

The following summary is given :—

" During the last two years my associates and I have observed a disease which seems to have been hitherto unknown in Palestine. The disorder is favism, an acute hemolytic anemia due to ingestion of broad beans (Vicia fava). Favism is not uncommon in Sicily and Sardinia ; only sporadic cases have occurred in other countries, for example, among Italian immigrants in the United States.

" The onset of the illness is sudden. The first symptoms are vomiting and diarrhoea. The urine is reddish-brown ; the skin turns pale gray ; the eyes become sunken, and consciousness is clouded. The number of erythrocytes may fall to 1,000,000 or less per cubic millimeter and the hemoglobin content to 10 per cent. Recovery, which begins spontaneously, in general is assisted by blood transfusions and takes one to two weeks. Fatalities are rare. The course of the illness resembles that of Lederer's anemia, but in favism relapses are common.

" Examination of the bone marrow suggests that there are a stoppage of the production of red blood cells during the hemolytic period and excessive production during the first days of recovery.

" We observed 6 patients with the disease ; 3 of them had two attacks. We believe that this disease is more common than is supposed and suggest that some of the patients with so-called blackwater fever may in reality suffer from favism."

W. Yorke.

SCHMIDT (G.). **Effect of Sun Stroke on the Central Nervous System.**—*Deut. Ztschr. f. Nervenheilk.* 1940. Vol. 151. pp. 146–152. [Summary taken from *Jl. Indust. Hyg. & Toxicol.* 1941. June. Vol. 23. No. 6. pp. 110–111. Signed L. Teleky.]

A soldier had a sun stroke in 1937 and suffered stiffness of the neck, paresis of the right arm and bradycardia. Severe headaches, tonic-clonic cramps, aphasia and right hemiplegia appeared a month later.

These symptoms improved slowly for 14 days but epileptic spasms occurred over longer periods. In December 1939, the man was hospitalized and displayed weakness, headache, dizziness and the deep re flexes on the right were more active than on the left. On the right side of the body, sensitivity to pain and temperature was diminished. Encephalography showed definite enlargement of both lateral ventricles, especially of the left, and of the third ventricle. The whole ventricular system was distorted to the left. The brain substance was atrophic, especially in the frontal lobe, and adhesions were present between the pia mater and the brain surface. The author believes that the sun stroke produced profound disturbance of the cerebral circulation. He stresses that such seemingly neurasthenic complaints have a true organic foundation.

Bohec (Joseph). Le coup de chaleur en mer. (Etude clinique, pathogénique et thérapeutique.) [**Heat Stroke at Sea.**]—*Ann. d'Hyg. Pub., Indust. et Sociale.* 1941. Sept.–Oct. Vol. 19. No. 5. pp. 204–216.

REVIEWS AND NOTICES.

Strickland (C.) [M.A., M.D., Fellow Royal Geographical Society, etc.]. **Deltaic Formation with Special Reference to the Hydrographic Processes of the Ganges and the Brahmaputra.** With a Foreword by Frank Debenham, O.B.E., M.A. and an Introduction by Cyril Fox, D.Sc., M.I.Min.E., etc.].—pp. xiii + 157. With 72 figs. & 1 map. 1940. London, New York & Toronto: Longmans, Green & Co., Ltd. [9s.]

During the last century there has been much controversy regarding the relation of the peculiar conditions arising from the changes in the course of the many mouths of the Ganges and Brahmaputra rivers, and the silting up of some of them, to the incidence of malaria in this large area. The author of this little book is a Calcutta medical entomologist who has closely studied the hydrography of this region, and describes it as a preliminary to a proposed sequel on the joint relationship of man and mosquitoes to the Bengal Delta. As pointed out in a foreword by a geologist, the Bengal area dealt with is not a true delta in the sense of the Nile and Mississippi, as the conditions are more complicated.

Although this volume deals solely with physical geography and geology the author betrays his medical interests in such headings, to some of the 27 sections into which he divides his subjects, as "The sea in pregnancy," "The birth and infancy of the land." He traces successively the deposition of alluvium brought down by the mighty rivers, the raising of the sea coast above the interior by tidal action, leaving a series of low-lying jheels or shallow lakes, behind the coast, the formation of the khals or outlets to the sea, the elevation of the river beds above the surrounding country with overspill of the water during the rains, etc. Tidal action, seasonal changes, underground flow of small rivers at the foot of the hills, seepage of water to the surface and the death of rivers through becoming silted up as the

main stream of the Ganges forced its way to the sea further and further to the East are all described. The last and longest section discusses geological theories to account for the extensive jheels and tracts which are below sea level; and the influence of "diastrophism of the earth's crust on the hydrographic processes." Here he rejects the view that the depressions are due to diastrophism or seismism.

In the work are reproduced many illustrations from geological and geographical books together with a number of explanatory diagrams. Some of these have had to be so much reduced as to require a magnifying glass for their study. It would have been advantageous if some of the technical terms had been more clearly defined, and many of the very numerous footnotes had been embodied in the text. The book should be read by those interested in the very special problem dealt with. The promised sequel will doubtless prove of greater interest to practitioners in the tropics, and especially to malariologists.

Leonard Rogers.

Rogers (Leonard) [K.C.S.I., C.I.E., LL.D., M.D., B.S., F.R.C.P., F.R.C.S., F.R.S., etc.] & Megaw (John W. D.) [K.C.I.E., B.A., M.B., Hon.D.Sc. (Queen's University, Belfast), etc.]. **Tropical Medicine.** Fourth Edition.—pp. xii+536. With 2 coloured plates & 87 text figs. 1942. London: J. & A. Churchill Ltd., 104 Gloucester Place, Portman Square. [21*s.*]

In general this edition maintains the form of its predecessors; the arrangement of the contents is much the same, length has been reduced by a few pages, and certain modifications have been introduced. But in spite of the apparent similarity it is evident that the authors have made considerable changes; there has been a good deal of rewriting, and room has been found for mention of most of the significant work which has appeared since the last edition was published. For instance, the recent work by Smith, Halder and Ahmed on the transmission of kala azar by sandflies, which has added emphatic support to a long held theory and has placed it on a basis almost of certainty, is recorded; in the same disease the new diagnostic method of gland puncture, and treatment by the stilbene group of drugs are not overlooked. Similarly, new work on the treatment of plague with sulphonamides is mentioned. Epidemic dropsy is discussed in the light of the Indian work which indicates that it is due to poisoning by the oil of *Argemone mexicana*, and in the same section, of diseases associated with diet, there is an expanded description of the nutritional anaemias. New tables of the classification of dietetic diseases, and of the vitamins together with the diseases associated with deficiency and the therapeutic doses of the isolated principles, have been added, and will facilitate reference and comprehension.

Some of the sections deal with diseases on which the authors are recognized authorities, and these, for instance cholera, leprosy, the typhus group and the dengue group, could hardly be bettered. In cholera the association of high relative humidity and epidemic outbreaks is fully discussed, and the problems of bacteriology and pathology are clearly set out. The description of fevers of the typhus group remains clear, and the classification is, perhaps, the most satisfactory that can yet be made of a complicated subject.

The helminthic diseases, as before, are confined to ankylostomiasis, the filarial diseases, and schistosomiasis; for practitioners in the Far

East it might be wise to add, in future editions, sections on infections with the common trematodes of those regions: *Clonorchis sinensis*, *Paragonimus ringeri* and *Fasciolopsis buski*.

The main interests of this text book are clinical and epidemiological. The needs of the clinician are, indeed, very fully met, and the book is a mine of information gathered largely from personal experience supported by wide knowledge of the literature. On the epidemiological side a suggestion might be offered that the complexities of anopheline transmission of malaria could be outlined more fully.

The book is better even than the former edition, and the high standards of learning and experience which have gone to its composition are evident throughout, but it remains concise and well ordered. The rapid exhaustion of the previous edition testifies to its value; the present edition can be even more fully recommended to all clinicians in hot countries.

C. W.

Muir (Robert) [M.A., M.D., Sc.D., LL.D., F.R.S., Emeritus Professor of Pathology, University of Glasgow, etc.]. **Text-Book of Pathology.** Fifth Edition.—pp. vii+991. With 599 figs. 1941. London: Edward Arnold & Co. [35*s*.] [This review appears also in *Bulletin of Hygiene*.]

Since the first appearance of this book in 1924, in addition to five reprints it has now reached the fifth edition. The work was written primarily as a text-book for students, and these facts are in themselves a sufficient testimonial to its popularity. Indeed "Muir" has already contributed to the education of many generations of students in pathology just as "Muir and Ritchie" did to that of previous generations in bacteriology. Here is condensed the unique knowledge which Sir Robert Muir has accumulated during a long life as teacher, observer and experimentalist and we have reason to be grateful for this permanent record of his experience. Thus the book becomes not only a text-book for students but also one which is a valuable addition to the shelves of all medical men, especially of those who have not access to a medical library.

The new edition has been brought completely up to date without any increase in length or considerable rearrangement of contents but with the addition of some 30 new text figures. The illustrations in general are much crisper than in previous editions and consist almost entirely of photographs or photomicrographs of actual specimens in the possession of the author or his colleagues. There is no doubt that this method of illustration is much to be preferred to the more elaborate diagrammatic or semi-diagrammatic pictures of some other (especially American) text-books. By the study of these figures the student can easily recall what he has actually seen in the *post-mortem* room and museum or under the microscope. The fount has been changed in the new edition, and this is a welcome improvement, though it may be mentioned in passing that the rather numerous printer's errors are an unfortunate occurrence.

In his preface to the first edition, Sir Robert explains that his book is based upon the course of instruction which he gave in Glasgow University, keeping in mind firstly the scientific aspect of general pathological processes and describing secondly those pathological changes which are of special importance in relation to clinical medicine

and surgery. Thus the early chapters are devoted to general considerations such as disturbances of the circulation, inflammation, repair, disturbances of nutrition, infection and tumours, while the later ones consist of descriptions of the diseases of each system in turn. Where, as in the field of cancer research, new knowledge and theories are being rapidly added to well-established facts, care has been taken to sift hypothesis from fact, with the result that a clear and succinct account of tumours and of the known aetiological factors in tumour growth is given. Similarly with diseases of the haemopoietic system. Following a very good description of the blood and the pathological changes which the component elements may undergo, is a simple yet fundamental classification of the anaemias and a clear account of these and the hyperplastic diseases, *i.e.* leukaemia and erythraemia. This section closes with a description of the haemorrhagic diseases.

Of necessity the chapters concerned with diseases of the reproductive system and endocrine glands are short but all the essential facts are there and reference is made to larger works where more detailed information can be obtained. Sir Robert's interest has, in recent years, been directed towards the study of cancer of the breast and thus the short section on this subject is of especial value.

In the chapter on Bright's disease, the author acknowledges his indebtedness to the writings of his pupil and colleague, Professor Shaw Dunn, whose work has contributed much to the elucidation of the mechanisms involved in this very difficult and complicated subject. After reading in addition the more recent publications of Professor Ellis (*Lancet*, 1942) it does seem as if we are now entering upon a new phase in the understanding of this complex of diseases.

This is not a text-book of tropical pathology but naturally there are many references to the diseases of warm climates, notably malaria, filariasis, cholera, dysentery, kala azar, leprosy and schistosomiasis. In addition some five pages are devoted to other helminthic parasites of man and their pathogenic effects, including hydatid disease. These short but pithy accounts provide most of what a student working for a medical qualification in these islands might reasonably be expected to know.

This is a book to be read and studied, not to be lightly skimmed. It is a mine of accurate information presented in ordered sequence—each paragraph planned and depending upon that preceding it, each argument developed step by step. Sir Robert Muir is to be congratulated and thanked for this new edition of his book.

Georgiana M. Bonser.

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